# SEARCH REQUEST FORM

**Scientific and Technical Information Center**

Requester's Full Name: Sabiha Qazi Examiner #: 74141 Date: 10/28/04
Art Unit: 1616 Phone Number 30 20622 Serial Number: 09/939,208
Mail Box and Bldg/Room Location: 4C70, Rem, 4A45 Results Format Preferred (circle): PAPER DISK E-MAIL

**If more than one search is submitted, please prioritize searches in order of need.**

**********

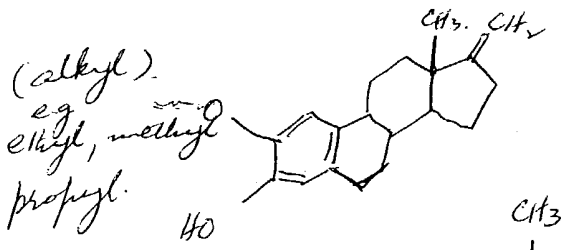
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Antiangiogenic Agents.

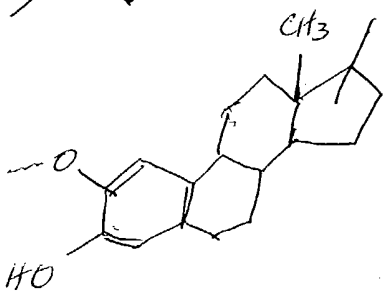
Inventors (please provide full names): Gregory E. Agoston, et al

Earliest Priority Filing Date: 8/24/01

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*




(cl 93)




(cl 94)

Please see attached sheets

Thanks

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| STAFF USE ONLY | | Type of Search | | Vendors and cost where applicable | |
|---|---|---|---|---|---|
| Searcher: | Jan | NA Sequence (#) | | STN | ✓ |
| Searcher Phone #: | 22504 | AA Sequence (#) | | Dialog | |
| Searcher Location: | | Structure (#) | ✓ | Questel/Orbit | |
| Date Searcher Picked Up: | 10/28 | Bibliographic | | Dr.Link | |
| Date Completed: | 10/28 | Litigation | | Lexis/Nexis | |
| Searcher Prep & Review Time: | | Fulltext | | Sequence Systems | |
| Clerical Prep Time: | 15 | Patent Family | | WWW/Internet | |
| Online Time: | 125 | Other | | Other (specify) | |

PTO-1590 (8-01)

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=> fil reg
FILE 'REGISTRY' ENTERED AT 14:03:30 ON 28 OCT 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   27 OCT 2004  HIGHEST RN 770693-70-4
DICTIONARY FILE UPDATES:  27 OCT 2004  HIGHEST RN 770693-70-4

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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L9                STR
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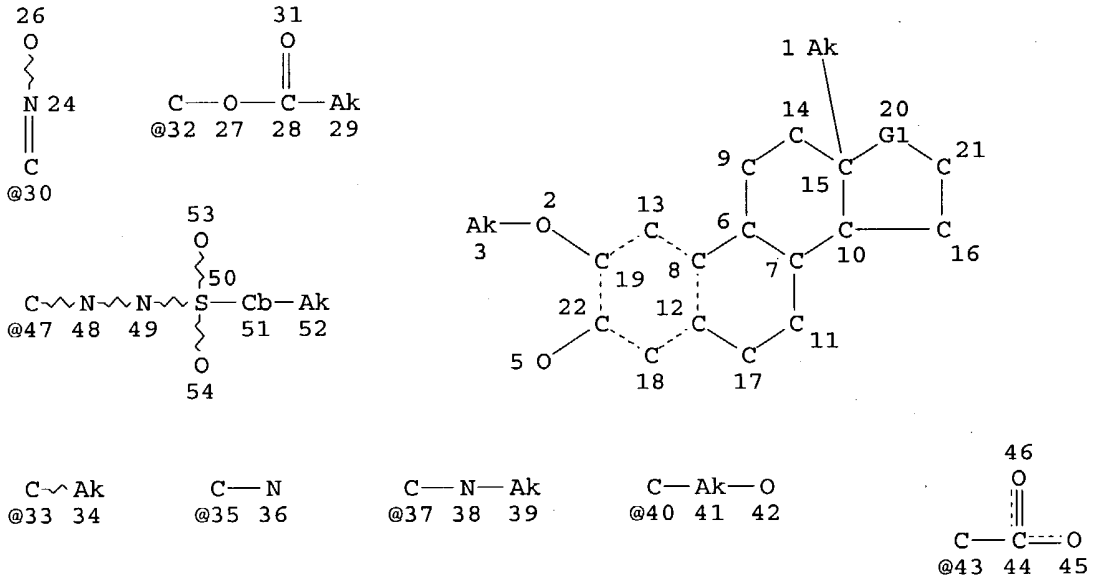








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VAR G1=33/30/32/37/40/43/47/35
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC  15
NUMBER OF NODES IS  51

STEREO ATTRIBUTES: NONE
L12          234 SEA FILE=REGISTRY SSS FUL L9
L13           32 SEA FILE=REGISTRY SUB=L12 CSS FUL L9

100.0% PROCESSED    234 ITERATIONS                    32 ANSWERS
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SEARCH TIME: 00.00.01

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L1             1 S US20020082433/PN
               SEL RN

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L2            68 S E1-E68
L3            63 S L2 AND C5-C6-C6-C6/ES
L4            19 S L3 AND 2/O
L5             1 S L4 AND C20H26O2
               E C20H26O2/MF
L6           146 S E3 AND 4432.3.65/RID
L7           146 S L6 AND 4/NR
L8             2 S L7 AND 2 METHOXY
L9             STR
L10            0 S L9 CSS SAM
L11           12 S L9 SAM
L12          234 S L9 FUL
               SAV TEMP QAZI939/A L12
L13           32 S L9 CSS FUL SUB=L12
               SAV TEMP L13 QAZI939A/A
L14           12 S L2 AND L13
L15           20 S L13 NOT L14
L16            3 S L15 AND (C21H28O4 OR C21H28O2)

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L17            0 S L14
L18            2 S L16
               SEL AN
               EDIT E1-E2 /OR
               EDIT /AN /OREF

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L20            2 S L19 NOT MAZUR ?/AU
L21            6 S L14
L22           11 S L16
L23           15 S L20-L22
L24            3 S L23 AND (AGOSTON G? OR SHAH J? OR HUNSUCKER K? OR PRIBLUDA V?
L25            2 S L23 AND ENTREMED?/PA,CS
L26            3 S L1,L24,L25
L27           12 S L23 NOT L26

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L28            4 S L14 OR L16

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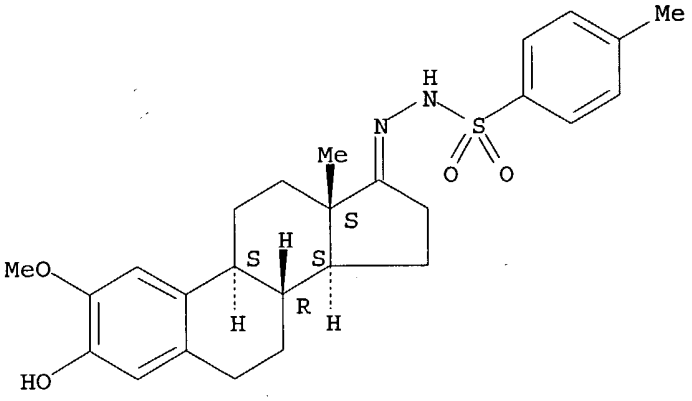
=> d ide can tot l14

L14 ANSWER 1 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN
RN **438044-29-2** REGISTRY
CN Benzenesulfonic acid, 4-methyl-, (3-hydroxy-2-methoxyestra-1,3,5(10)-trien-

17-ylidene)hydrazide (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H32 N2 O4 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.
Double bond geometry unknown.



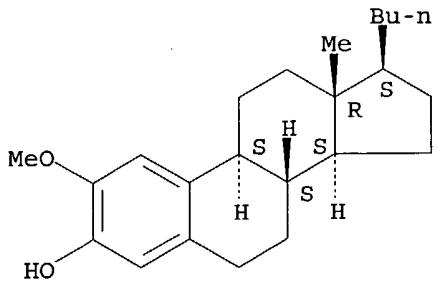

**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:47357

L14 ANSWER 2 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN
RN **431901-78-9** REGISTRY
CN 19,21-Dinorchola-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H34 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

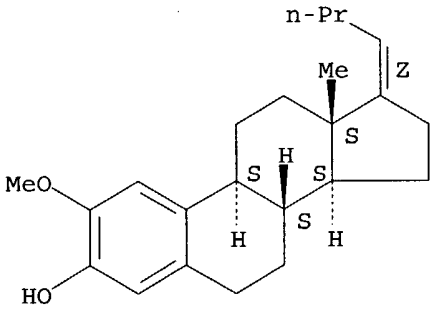
REFERENCE 1: 139:224972

REFERENCE 2: 137:47357

REFERENCE 3: 137:6309

L14 ANSWER 3 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN
RN **431901-77-8** REGISTRY
CN 19,21-Dinorchola-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H32 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.
Double bond geometry as shown.




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:224972

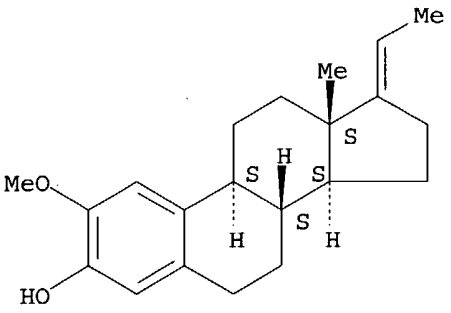
REFERENCE 2: 137:47357

REFERENCE 3: 137:6309

L14 ANSWER 4 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN
RN **431901-75-6** REGISTRY
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C21 H28 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.

Double bond geometry unknown.

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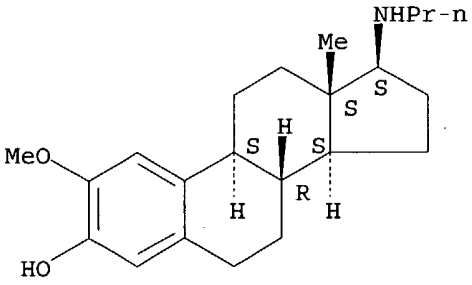
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 137:47357

REFERENCE 2: 137:6309

L14 ANSWER 5 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN
RN **431901-74-5** REGISTRY
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-(propylamino)-, (17β)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C22 H33 N O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

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2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

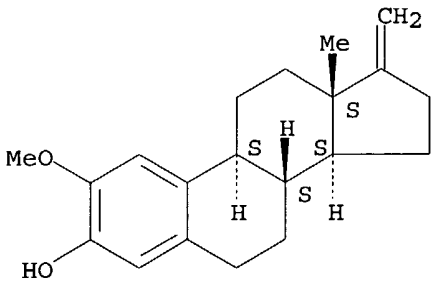
REFERENCE 1: 137:47357

REFERENCE 2: 137:6309

L14 ANSWER 6 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN
RN **431901-73-4** REGISTRY

CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methylene- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2-Methoxy-17(20)-methyleneestra-1,3,5(10)-trien-3-ol
CN 3-Hydroxy-2-methoxy-17(20)-methyleneestra-1,3,5(10)-triene
FS STEREOSEARCH
MF C20 H26 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.

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4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:243723

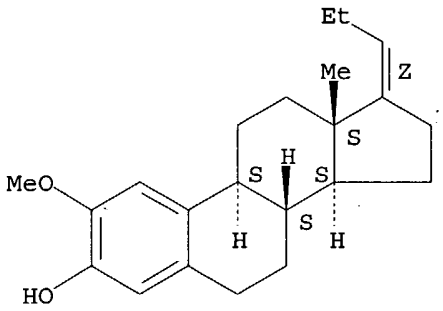
REFERENCE 2: 140:73598

REFERENCE 3: 137:47357

REFERENCE 4: 137:6309

L14 ANSWER 7 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN
RN **431901-72-3** REGISTRY
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propylidene-, (17Z)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C22 H30 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.
Double bond geometry as shown.




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

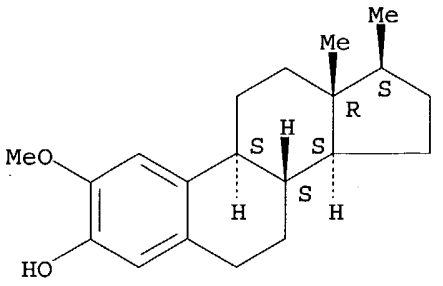
REFERENCE 1: 139:224972

REFERENCE 2: 137:47357

REFERENCE 3: 137:6309

L14 ANSWER 8 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN
RN **431901-71-2** REGISTRY
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methyl-, (17β)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2-Methoxy-17β-methylestra-1,3,5(10)-trien-3-ol
CN 3-Hydroxy-2-methoxy-17β-methylestra-1,3,5(10)-triene
FS STEREOSEARCH
MF C20 H28 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.

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REFERENCE 1: 141:243723

REFERENCE 2: 139:224972

REFERENCE 3: 137:47357

REFERENCE 4: 137:6309

L14 ANSWER 9 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN
RN **431901-70-1** REGISTRY
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FS STEREOSEARCH
MF C22 H32 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
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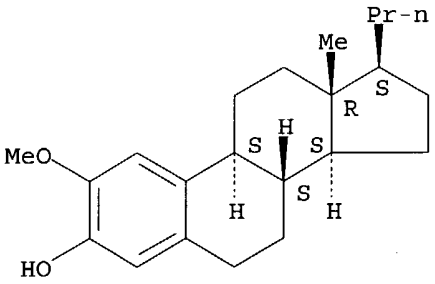
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

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3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:224972

REFERENCE 2: 137:47357

REFERENCE 3: 137:6309

L14 ANSWER 10 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN
RN **431901-69-8** REGISTRY
CN Estra-1,3,5(10)-trien-17-one, 3-hydroxy-2-methoxy-, oxime (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C19 H25 N O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
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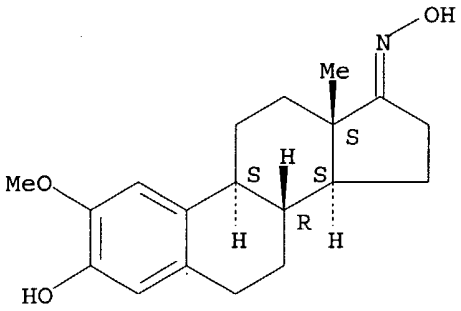
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.
Double bond geometry unknown.




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

3 REFERENCES IN FILE CA (1907 TO DATE)
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:224972

REFERENCE 2: 137:47357

REFERENCE 3: 137:6309

L14 ANSWER 11 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN
RN **431901-68-7** REGISTRY
CN Estra-1,3,5(10)-trien-3-ol, 17-amino-2-methoxy-, (17β)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C19 H27 N O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
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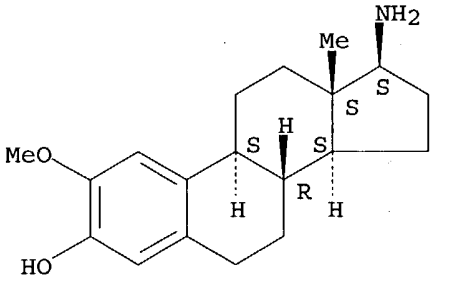
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.

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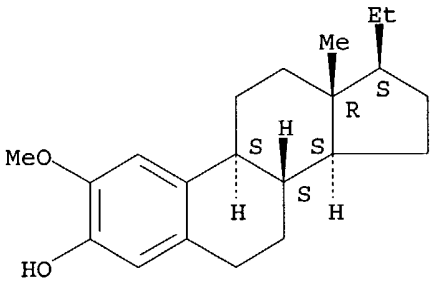
REFERENCE 1: 139:224972

REFERENCE 2: 137:47357

REFERENCE 3: 137:6309

L14 ANSWER 12 OF 12 REGISTRY COPYRIGHT 2004 ACS on STN
RN **229486-18-4** REGISTRY
CN 19-Norpregna-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C21 H30 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

Absolute stereochemistry.




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

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4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:224972

REFERENCE 2: 137:47357

REFERENCE 3: 137:6309

REFERENCE 4: 131:88083

=> d ide can tot l16

L16 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN
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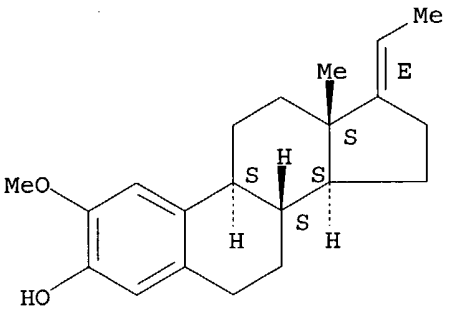
FS STEREOSEARCH
MF **C21 H28 O2**
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation)

Absolute stereochemistry.
Double bond geometry as shown.

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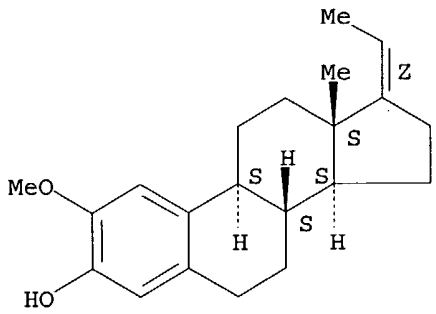
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:224972

L16 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN
RN 229486-17-3 REGISTRY
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C21 H28 O2**
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.
Double bond geometry as shown.

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5 REFERENCES IN FILE CA (1907 TO DATE)
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REFERENCE 1: 140:73598

REFERENCE 2: 137:370278

REFERENCE 3: 135:358085

REFERENCE 4: 133:350395

REFERENCE 5: 131:88083

L16 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN
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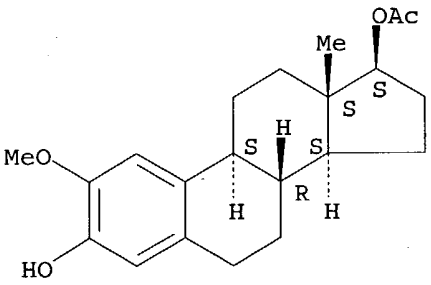
CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, 17-acetate, (17β)-
(9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Estradiol, 2-methoxy-, 17-acetate (6CI)
FS STEREOSEARCH
MF **C21 H28 O4**
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, TOXCENTER
(*File contains numerically searchable property data)
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent); NORL (No role in record)

Absolute stereochemistry.




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

5 REFERENCES IN FILE CA (1907 TO DATE)
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 139:369731

REFERENCE 2: 134:295993

REFERENCE 3: 88:121515

REFERENCE 4: 81:4163

REFERENCE 5: 54:97743

=> fil hcaold
FILE 'HCAOLD' ENTERED AT 14:03:52 ON 28 OCT 2004
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FILE LAST UPDATED: 01 May 1997 (19970501/UP)

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assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

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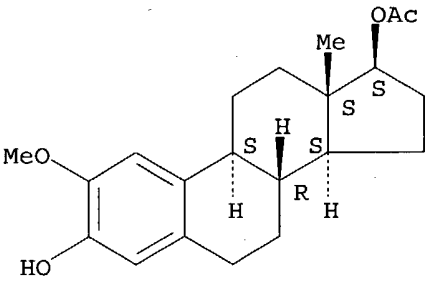
=> d all hitstr tot l18

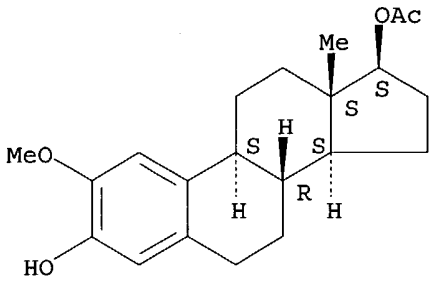
L18 ANSWER 1 OF 2 HCAOLD COPYRIGHT 2004 ACS on STN
AN CA54:18587f CAOLD
TI catechol derivs. of estrogens
AU Fishman, Jack; Tomasz, M.; Lehman, R.
TI studies using anterior pituitary hormones as antigens
AU Fishman, Joseph; McGarry, E. E.; Beck, J. C.
IT 1236-72-2 5976-64-7 5976-65-8 5976-67-0 5976-70-5 21696-98-0
23463-05-0 28818-82-8 **52717-98-3** 52717-99-4 59495-33-9
116282-36-1 117921-01-4 121176-83-8 121212-59-7 121212-60-0 122426-55-5
IT **52717-98-3**
RN 52717-98-3 HCAOLD
CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, 17-acetate, (17β)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.




L18 ANSWER 2 OF 2 HCAOLD COPYRIGHT 2004 ACS on STN
AN CA52:13765i CAOLD
TI synthesis of 2-methoxyestrogens
AU Fishman, Jack
IT 362-07-2 362-08-3 7291-57-8 38781-50-9 **52717-98-3**
65932-49-2 65932-50-5 65932-51-6 65932-52-7 65932-53-8 84509-93-3
103278-44-0 120024-00-2
IT **52717-98-3**
RN 52717-98-3 HCAOLD
CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, 17-acetate, (17β)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.




=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 14:05:22 ON 28 OCT 2004
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FILE COVERS 1907 - 28 Oct 2004 VOL 141 ISS 18
FILE LAST UPDATED: 27 Oct 2004 (20041027/ED)

This file contains CAS Registry Numbers for easy and accurate
substance identification.

=> d all hitstr tot l30

L30 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1960:97743 HCAPLUS
DN 54:97743
OREF 54:**18587e-i,18588a-e**
ED Entered STN: 22 Apr 2001
TI Catechol derivatives of estrogens
AU Fishman, Jack; Tomasz, Maria; Lehman, Rosemarie
CS Sloan-Kettering Inst. for Cancer Research, New York, NY
SO Journal of Organic Chemistry (1960), 25, 585-8
CODEN: JOCEAH; ISSN: 0022-3263
DT Journal
LA Unavailable
CC 10J (Organic Chemistry: Steroids)
OS CASREACT 54:97743
AB Prepns. of 2-methoxyestriol (I), 2-hydroxyestriol (II) 3-Me ether (III), 2-hydroxyestradiol (IV) 3-Me ether (V), 2-methoxyestrone 3-Me ether (VI), and 2-hydroxyestrone (VII), with various derivs. and intermediates were described. Estriol (8.3 g.) in 250 ml. 95% alc. containing 1.5 g. KOH refluxed 48 hrs. with 6.5 g. 2-chloro-5-nitrobenzophenone, acidified to pH 3, extracted continuously 24 hrs. with Et2O, the extract evaporated and the product chromatographed on Al2O3 gave 5.6 g. crude material and 1.5 g. unchanged estriol. The product on recrystn. gave 16α,17β-dihydroxy-

[α]28D 89°. XIII (240 mg.) in 20 cc. piperidine refluxed 1 hr., cooled, diluted with 100 cc. C6H6, washed with dilute H2SO4, dried, evaporated, the residual oil subjected to a 99-transfer countercurrent distribution between 70% aqueous MeOH and CCl4, and the combined tubes 14-32 filtered through Al2O3 and crystallized from aqueous MeOH gave 108 mg. 2-methoxyestrone, blades, m. 188-91°, giving with NaOH and BzCl the 3-monobenzoate, needles, m. 225-8°, which was also obtained by oxidation of XI with CrO3.

IT Estra-1,3,5(10)-trien-17β-ol, 3-(2-benzoyl-4-nitrophenoxy)-
Estra-1,3,5(10)-trien-17β-ol, 3-(2-benzoyl-4-nitrophenoxy)-, acetate
Estra-1,3,5(10)-trien-17β-ol, 3-(2-benzoyl-4-nitrophenoxy)-2-methoxy-
Estra-1,3,5(10)-trien-17β-ol, 3-(2-benzoyl-4-nitrophenoxy)-2-methoxy-, acetate

IT 362-07-2, Estradiol, 2-methoxy-
(and derivs.)

IT 362-08-3, Estrone, 2-methoxy- 38781-50-9, Benzophenone, 2-(2,17β-dihydroxyestra-1,3,5(10)-trien-3-yloxy)-5-nitro-, 17-acetate 65932-49-2, Benzophenone, 2-(17β-hydroxyestra-1,3,5(10)-trien-3-yloxy)-5-nitro- 65932-50-5, Benzophenone, 2-(17β-hydroxyestra-1,3,5(10)-trien-3-yloxy)-5-nitro-, acetate 65932-51-6, Benzophenone, 2-(17β-hydroxy-2-methoxyestra-1,3,5(10)-trien-3-yloxy)-5-nitro-, acetate 65932-52-7, Benzophenone, 2-(17β-hydroxy-2-methoxyestra-1,3,5(10)-trien-3-yloxy)-5-nitro- 65932-53-8, Estra-1,3,5(10)-trien-17-one, 3-(2-benzoyl-4-nitrophenoxy)-2-methoxy- 103278-44-0, Estra-1,3,5(10)-trien-17-one, 3-(2-benzoyl-4-nitrophenoxy)- 120024-00-2, Estrone, 2-methoxy-, benzoate
(preparation of)

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=> s l27 not l30
L31          10 L27 NOT L30

=> d all hitstr tot

L31  ANSWER 1 OF 10  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:718556  HCAPLUS
DN   141:243723
ED   Entered STN:  02 Sep 2004
TI   Preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an
     antitumor action
IN   Hillisch, Alexander; Peters, Olaf; Gege, Christian; Regenhardt, Wilko;
     Kosemund, Dirk; Siemeister, Gerhard; Unger, Eberhard; Bothe, Ulrich
PA   Schering Aktiengesellschaft, Germany
SO   PCT Int. Appl., 47 pp.
     CODEN: PIXXD2
DT   Patent
LA   German
IC   ICM  C07J041-00
     ICS  A61K031-565; A61P035-00
CC   32-3 (Steroids)
     Section cross-reference(s): 1, 2, 63
FAN.CNT 1
     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
PI   WO 2004074307         A1    20040902    WO 2004-EP1606          20040219
         W:  AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG,
             BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR,
             CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES,
             ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN,
             IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC,
             LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX,
             MZ, MZ, NA, NI
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
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BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG

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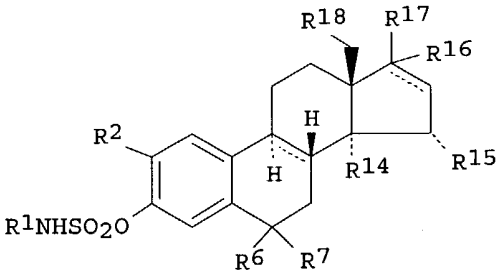
|---|---|---|---|---|---|
| | DE 10307104 | A1 | 20040923 | DE 2003-10307104 | 20030219 |
| PRAI | DE 2003-10307104 | A | 20030219 | | |

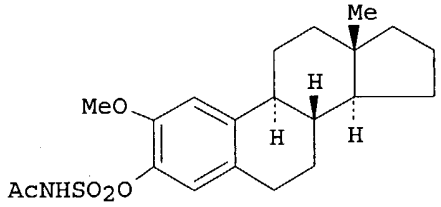
CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---|---|---|
| WO 2004074307 | ICM | C07J041-00 |
| | ICS | A61K031-565; A61P035-00 |

GI




I




II

AB The invention relates to the use of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates I [R1 = H, C1-5-alkyl, C1-5-acyl; R2 = C1-5-alkoxy, C1-5-alkyl, O-CnFmHo, with the proviso that if R2 = alkyl, then R17 = C1-5-alkoxy; n = 1 - 6, m > 1, m + o = 2n + 1; R6 = H; R7 = H, OH, NH2, NH-acyl (with the proviso, that when R6 ≠ H and R7 ≠ H, then R17 = C1-5-alkoxy); R6R7 = O, NOH, NO-(C1-5-alkyl); R14, R15 = H; R14R15 = CH2, bond; R16 = H, F, C1-5-alkyl, R17 = H, F, C1-5-alkoxy (with the proviso that when R16 = H, R17 = CHXY where X = H, F, C1-4-alkyl; Y = H, F; if X = F, then Y = H, F; if X = OH, then Y = H; XY = O; if R16 = F, then R17 = H or F); R16R17 = :CAB; A, B = H, F, C1-5-alkyl; R18 = H, Me (with the proviso that when R18 = Me, then R17 = SO3NHR1); dashed line = single or double bond], in addition to their pharmaceutically acceptable salts for producing a medicament. Thus, 2-methoxyestra-1,3,5(10)-trien-3-yl N-acetylsulfamate (II) was prepared from 2-methoxyestra-1,3,5(10)-trien-3-ol via sulfamoylation with ClSO2NH2 in CH2Cl2 containing 2,6-di(tert-butyl)pyridine followed by acetylation with acetic anhydride. Said compds. have an antitumor action [for N-desacetyl II; IC50 = 0.67 μM for inhibition of tubulin polymerization; IC50 = 0.4 μM vs. NCI-H460 (lung carcinoma ATCC HTB-177); IC50 = 0.4 μM vs. HCT116 (colon cancer ATCC

CCL-247); IC50 = 0.5 μM vs. DU145 (prostate cancer ATCC HTB-81); IC50 = 0.11 μM vs. MaTu/ADT (breast cancer Epo GmbH Berlin); IC50 = <0.1 μM vs. HMVEC (endothelial cells)] .

ST estratrienyl sulfamate deriv prepn antitumor tubulin polymn inhibitor; breast cancer inhibitor estratrienyl sulfamate deriv prepn

IT Endothelium
(antiproliferants; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT Mammary gland, neoplasm
Prostate gland, neoplasm
(carcinoma, medicinals; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT Intestine, neoplasm
(colon, medicinals; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT Cell proliferation
(inhibition; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT Lung, neoplasm
Mammary gland, neoplasm
Reproductive organ, neoplasm
(medicinals; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT Tubulins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(polymerization, inhibition; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT Antitumor agents
Cytotoxic agents
Human
(preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT Estrogens
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT 362-08-3, 3-Hydroxy-2-methoxyestra-1,3,5(10)-trien-17-one
RL: RCT (Reactant); RACT (Reactant or reagent)
(Wittig methylenation or Grignard reaction of, with allylmagnesium bromide; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT 752246-14-3, 3-Acetoxy-2-methoxy-18a-homoestra-1,3,5(10)-triene
RL: RCT (Reactant); RACT (Reactant or reagent)
(benzylic oxidation of, with chromium trioxide; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT 752246-09-6, 3-Acetoxy-2-methoxy-17(20)-methylene-6-oxoestra-1,3,5(10)-triene
RL: RCT (Reactant); RACT (Reactant or reagent)
(deacetylation and sulfamoylation of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

IT 185910-34-3, 2-Methoxy-17-oxoestra-1,3,5(10)-trien-3-yl sulfamate
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(oximation of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)

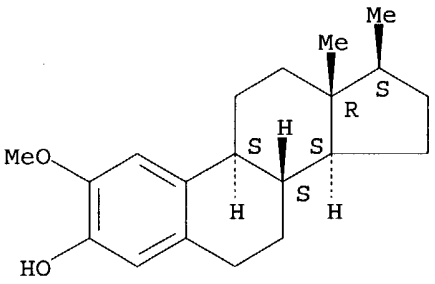
IT 208924-88-3DP, Estra-1,3,5(10)-triene-3-yl sulfamate, derivs.
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acylation of, with anhydrides; preparation of 2-substituted

estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
IT 752246-13-2P, 17α-(Azidomethyl)-3,17β-dihydroxy-2-methoxyestra-1,3,5(10)-triene
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and azide reduction of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
IT 752245-83-3P, 2-Methoxy-17(20)-methylene-6-oxoestra-1,3,5(10)-trien-3-yl sulfamate
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation and benzylic oxidation of, with chromium oxide; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
IT 752246-07-4P, 2-(1-Methoxyethyl)-3-(benzyloxy)-17β-methoxyestra-1,3,5(10)-triene
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolysis of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
IT 752245-92-4P, 2-Methoxy-6-oxo-18a-homoestra-1,3,5(10)-trien-3-yl sulfamate
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation and reduction or oximation of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
IT 748807-33-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction or sulfamoylation of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
IT 752246-12-1P, 3-Hydroxy-2-methoxyestra-1,3,5(10)-triene-17β-spiro-1',2'-oxiran
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and regioselective azidation of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
IT 752246-06-3P, 17α-Allyl-2-methoxyestra-1,3,5(10)-trien-3,17β-diol
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and sulfamoylation of, with sulfamoyl chloride; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
IT **431901-71-2P**, 3-Hydroxy-2-methoxy-17β-methylestra-1,3,5(10)-triene 752246-08-5P, 2-Ethyl-3-hydroxy-17β-methoxyestra-1,3,5(10)-triene 752246-11-0P, 17β-Difluoromethyl-3-hydroxy-2-methoxyestra-1,3,5(10)-triene 752246-15-4P, 17α-Fluoro-3-hydroxy-2-methoxyestra-1,3,5(10)-triene
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and sulfamoylation of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
IT **431901-73-4P**, 3-Hydroxy-2-methoxy-17(20)-methyleneestra-1,3,5(10)-triene 752246-10-9P, 17(20)-Difluoromethylene-3-hydroxy-2-methoxyestra-1,3,5(10)-triene
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and sulfamoylation or stereoselective hydrogenation of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an

antitumor action)
IT 33069-62-4, Taxol
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
IT 748807-30-9P 748807-31-0P 748807-32-1P 752245-75-3P, 2-Methoxyestra-1,3,5(10)-trien-3-yl sulfamate 752245-76-4P, 2-Methoxyestra-1,3,5(10)-trien-3-yl N-acetylsulfamate 752245-77-5P, 2-Methoxy-6-(oximino)estra-1,3,5(10)-trien-3-yl sulfamate 752245-78-6P, 2-Methoxyestra-1,3,5(10),16-tetraen-3-yl sulfamate 752245-79-7P, 2-Methoxy-17-[(E)-vinylmethylene]estra-1,3,5(10)-trien-3-yl sulfamate 752245-80-0P, 2-Ethyl-17β-methoxyestra-1,3,5(10)-trien-3-yl sulfamate 752245-81-1P, 2-Methoxy-17(20)-methyleneestra-1,3,5(10)-trien-3-yl sulfamate 752245-82-2P, 2-Methoxy-17β-methylestra-1,3,5(10)-trien-3-yl sulfamate 752245-84-4P, 2-Methoxy-17(20)-methylene-6-oximinoestra-1,3,5(10)-trien-3-yl sulfamate 752245-85-5P, 17(20)-Difluoromethylene-2-methoxyestra-1,3,5(10)-trien-3-yl sulfamate 752245-86-6P, 17β-Difluoromethyl-2-methoxyestra-1,3,5(10)-trien-3-yl sulfamate 752245-87-7P, 2-Methoxyestra-1,3,5(10),14-tetraen-3-yl sulfamate 752245-88-8P, 17,17-Difluoro-2-methoxyestra-1,3,5(10),14-tetraen-3-yl sulfamate 752245-89-9P, 17,17-Difluoro-2-methoxy-18a-homoestra-1,3,5(10),14-tetraen-3-yl sulfamate 752245-90-2P, 17β-Formyl-2-Methoxy-18a-homoestra-1,3,5(10)-trien-3-yl sulfamate 752245-91-3P, 17β-Hydroxymethyl-2-methoxyestra-1,3,5(10)-trien-3-yl sulfamate 752245-93-5P, 2-Methoxy-6-oximino-18a-homoestra-1,3,5(10)-trien-3-yl sulfamate 752245-94-6P, 2-Methoxy-6-(O-methyloximino)-18a-homoestra-1,3,5(10)-trien-3-yl sulfamate 752245-95-7P, 6α-Acetylamino-2-methoxy-18a-homoestra-1,3,5(10)-trien-3-yl sulfamate 752245-96-8P, 6α-Hydroxy-2-methoxy-18a-homoestra-1,3,5(10)-trien-3-yl sulfamate 752245-97-9P, 17α-Fluoro-2-methoxyestra-1,3,5(10)-trien-3-yl sulfamate 752245-98-0P, 17β-Fluoro-2-methoxyestra-1,3,5(10)-trien-3-yl sulfamate 752245-99-1P, 17,17-Difluoro-2-methoxyestra-1,3,5(10)-trien-3-yl sulfamate 752246-00-7P, 17,17-Difluoro-2-methoxy-6-oximinoestra-1,3,5(10)-trien-3-yl sulfamate 752246-01-8P, 17,17-Difluoro-2-methoxy-18a-homoestra-1,3,5(10)-trien-3-yl sulfamate 752246-02-9P, 17,17-Difluoro-2-methoxy-6-oximino-18a-homoestra-1,3,5(10)-trien-3-yl sulfamate 752246-03-0P, 17,17-Difluoro-2-methoxyestra-1,3,5(10)-trien-3-yl N-acetylsulfamate 752246-04-1P, 2-Methoxy-17-[(E)-oximino]estra-1,3,5(10)-trien-3-yl sulfamate 752246-05-2P, 17α-Allyl-17β-hydroxy-2-methoxyestra-1,3,5(10)-trien-3-yl sulfamate
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
IT 362-07-2, 2-Methoxyestra-1,3,5(10)-triene-3,17β-diol
RL: RCT (Reactant); RACT (Reactant or reagent)
(regioselective fluorination of, with DAST; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
IT 26357-04-0, 2-Acetyl-3-(benzyloxy)estra-1,3,5(10)-trien-17-one
RL: RCT (Reactant); RACT (Reactant or reagent)
(stereoselective reduction and O-methylation of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
IT 1217-09-0D, Estra-1,3,5(10)-triene, derivs. 4953-96-2, 2-Methoxyestra-1,3,5(10)-trien-3-ol
RL: RCT (Reactant); RACT (Reactant or reagent)
(sulfamoylation of, with sulfamoyl chloride; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Ina, S; WO 0118028 A 2001
(2) Maccarthy-Morrogh, L; CANCER RESEARCH 2000, V60(19), P5441 HCAPLUS

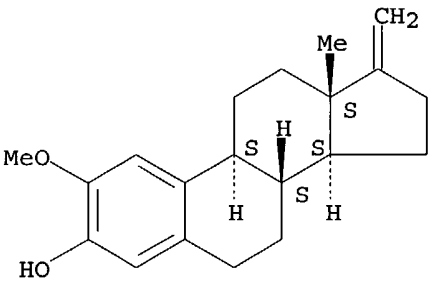
(3) Purohit, A; JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY 1999, V69(1/6), P227
(4) Singh, A; MOLECULAR AND CELLULAR ENDOCRINOLOGY 2000, V160, P61 HCAPLUS
(5) Stanford Res Inst Int; WO 9933858 A 1999 HCAPLUS
IT **431901-71-2P**, 3-Hydroxy-2-methoxy-17β-methylestra-1,3,5(10)-triene
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and sulfamoylation of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
RN 431901-71-2 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methyl-, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




IT **431901-73-4P**, 3-Hydroxy-2-methoxy-17(20)-methyleneestra-1,3,5(10)-triene
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and sulfamoylation or stereoselective hydrogenation of; preparation of 2-substituted estra-1,3,5(10)-trien-3-yl sulfamates with an antitumor action)
RN 431901-73-4 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




L31 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:3558 HCAPLUS
DN 140:73598
ED Entered STN: 04 Jan 2004
TI Systems and methods for rapid evaluation and design of molecules for predicted biological activity
IN Hendry, Lawrence B.
PA USA
SO U.S. Pat. Appl. Publ., 44 pp.

CODEN: USXXCO
DT Patent
LA English
IC ICM A01N001-00
NCL 435001100
CC 9-16 (Biochemical Methods)
Section cross-reference(s): 1, 3
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2004002052 | A1 | 20040101 | US 2002-279546 | 20021023 |
| PRAI | US 2001-344560P | P | 20011023 | | |
| | US 2001-339954P | P | 20011210 | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---|---|---|
| US 2004002052 | ICM | A01N001-00 |
| | NCL | 435001100 |

AB The computer-based systems and methods are for rapidly evaluating mols. for suspected biol. activity and relative potency, and for designing mols. for desired biol. activity. The systems and methods enable rapid screening of large mol. databases using one or more search engines designed to identify mols. predicted to possess specific biol. activities. Estradiol, 8 other estrogens and the conformation of the DNA site into which they fit were used to construct a search engine which was used to search databases containing a variety of compound structures.

ST system rapid evaluation design mol predicted biol activity; computer system design evaluation biol activity; large mol database search engine biol activity; estrogen search engine screening

IT Named reagents and solutions
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Horeau's acid, identified by estrogenic search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Antibiotics
(against anthrax, evaluation of substances for predicted activity of; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Bacillus anthracis
(anthrax from, antibiotics against, evaluation of substances for predicted activity of; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Electrostatic potential
(between mol. and binding site, in creating search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Nucleic acids
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(creating search engines for mols. binding specified sites in; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Penis
(erectile activity, evaluation of substances for; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT Angiogenesis inhibitors
Antidepressants
Antidiabetic agents
Carcinogens
Hypnotics and Sedatives
Selective estrogen receptor modulators
(evaluation of substances for predicted activity of; systems and methods for rapid evaluation and design of mols. for predicted biol.

activity)
IT Androgens
Estrogens
Glucocorticoids
Progestogens
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(evaluation of substances for predicted activity of; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)
IT Bone
Thyroid gland
(evaluation of substances for predicted activity on; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)
IT Sexual behavior
(impotence, evaluation of substances for predicted erectile activity and treatment of; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)
IT Databases
(large mol., systems and methods and search engines for rapid screening of; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)
IT Information systems
(network; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)
IT Information systems
(searching; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)
IT Apparatus
Bioinformatics
Computer program
Computers
Conformation
Data processing
Design
Drug design
Excluded volume
Functional groups
Hydrogen bond
Molecular shape
Molecular surface
Molecules
Simulation and Modeling, biological
Simulation and Modeling, physicochemical
Structure-activity relationship
Volume
(systems and methods for rapid evaluation and design of mols. for predicted biol. activity)
IT DNA
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(systems and methods for rapid evaluation and design of mols. for predicted biol. activity)
IT 388075-75-0, PDC 7
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(PDC 7, identified by estrogenic search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)
IT 58-22-0, Testosterone 434-22-0, 19-Nortestosterone 521-11-9, 17α-Methyl-5α-dihydrotestosterone 521-18-6, 5α Dihydrotestosterone 1434-85-1, 5α-Dihydro-19-nortestosterone 3704-07-2, 7α-Methyl-5α-dihydrotestosterone 3704-08-3 3764-87-2, 7α-Methyl-19-nortestosterone 6424-04-0 7642-58-2,

7α-Methyltestosterone 31025-34-0
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as standard in construction of search engine for evaluation of substances for predicted androgenic activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 389-08-2, Nalidixic acid 70458-92-3, Pefloxacin 70458-96-7, Norfloxacin 79660-72-3, Fleroxacin 85721-33-1, Ciprofloxacin 98079-51-7, Lomefloxacin 100986-85-4, Levofloxacin 110871-86-8, Sparfloxacin 112811-59-3, Gatifloxacin 147059-72-1, Trovafloxacin 151096-09-2, Moxifloxacin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as standard in construction of search engine for evaluation of substances for predicted anthrax antibiotic activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 362-07-2, 2-Methoxyestradiol 165619-07-8, 2-Ethoxyestradiol 192062-02-5 **229486-17-3 431901-73-4** 431901-98-3 431902-09-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as standard in construction of search engine for evaluation of substances for predicted antiangiogenic activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 50-48-6, Amitriptyline 50-49-7, Imipramine 303-49-1 5560-72-5, Iprindole 10262-69-8, Maprotiline 24526-64-5, Nomifensin 54910-89-3, Fluoxetine 79617-96-2, Sertraline
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as standard in construction of search engine for evaluation of substances for predicted antidepressant activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 50-28-2, Estradiol, biological studies 57-63-6, 17α-Ethynylestradiol 4567-67-3, 17α-Chloroethynylestradiol 21507-14-2, 11β-Methoxyestradiol 34816-55-2, Moxestrol 95258-49-4 95258-51-8 108887-25-8 130929-98-5 164580-56-7
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as standard in construction of search engine for evaluation of substances for predicted estrogenic activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 50-23-7, Cortisol
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as standard in construction of search engine for evaluation of substances for predicted glucocorticoid activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 53-43-0, Dehydroepiandrosterone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as standard in construction of search engine for evaluation of substances for predicted penile erectile and anti-impotence activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 516-54-1, 3α, 5α-Tetrahydroprogesterone 516-55-2 23930-19-0, Alphaxalone 38398-32-2, Ganaxolone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as standard in construction of search engine for evaluation of substances for predicted sedative activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 15178-66-2
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(dbl. stranded, as DNA binding site used in evaluation of substances for predicted anthrax antibiotic activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 4251-20-1
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(dbl. stranded, as DNA binding site used in evaluation of substances

for predicted estrogenic or androgenic or other activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 3704-09-4, Mibolerone
RL: BSU (Biological study, unclassified); BIOL (Biological study) (identified by androgen search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 69-53-4, Ampicillin 28657-80-9, Cinoxacin
RL: BSU (Biological study, unclassified); BIOL (Biological study) (identified by anthrax antibiotic search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 54-32-0, Moxisylyte 56-87-1, Lysine, biological studies 74-79-3, Arginine, biological studies 497-76-7, Arbutin 2530-97-4, Xanthinol 7665-99-8, Cyclic GMP
RL: BSU (Biological study, unclassified); BIOL (Biological study) (identified by anti-impotence search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 117-39-5, Quercetin 501-36-0, Resveratrol 26581-81-7, EM-12
RL: BSU (Biological study, unclassified); BIOL (Biological study) (identified by antiangiogenic search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 17692-37-4, Fantridone 34911-55-2, Bupropion 54739-18-3, Fluvoxamine 71620-89-8, Reboxetine 93413-69-5, Venlafaxine
RL: BSU (Biological study, unclassified); BIOL (Biological study) (identified by antidepressant search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 124-87-8, Picrotoxin 5938-11-4, Callicarpone 20071-51-6, Eupatoroxin
RL: BSU (Biological study, unclassified); BIOL (Biological study) (identified by carcinogenic search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 24643-97-8, Indenestrol
RL: BSU (Biological study, unclassified); BIOL (Biological study) (identified by estrogen search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 56-53-1, trans-Diethylstilbestrol 446-72-0, Genistein 486-66-8, Daidzein 531-95-3, Equol 26538-44-3, Zearalanol
RL: BSU (Biological study, unclassified); BIOL (Biological study) (identified by estrogenic search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 50-35-1, Thalidomide
RL: BSU (Biological study, unclassified); BIOL (Biological study) (identified by sedative and antidepressant and antiangiogenic search engines; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT 21715-46-8, Etifoxine 61869-08-7, Paroxetine
RL: BSU (Biological study, unclassified); BIOL (Biological study) (identified by sedative and antidepressant search engines; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

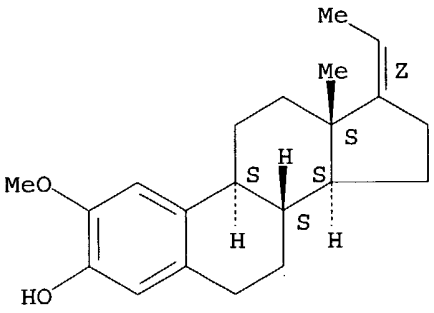
IT 57-43-2, Amobarbital 58-61-7, Adenosine, biological studies 73-31-4, Melatonin 77-26-9, Butalbital 1972-08-3, δ9 Tetrahydrocannabinol 20007-85-6, Cyclopenol 57801-81-7, Brotizolam
RL: BSU (Biological study, unclassified); BIOL (Biological study) (identified by sedative search engine; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

IT **229486-17-3 431901-73-4**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (as standard in construction of search engine for evaluation of substances for predicted antiangiogenic activity; systems and methods for rapid evaluation and design of mols. for predicted biol. activity)

RN 229486-17-3 HCAPLUS

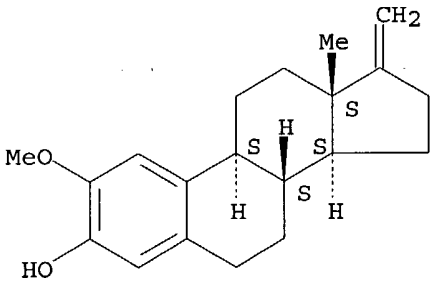
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.




RN 431901-73-4 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




L31 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:892536 HCAPLUS
DN 139:369731
ED Entered STN: 14 Nov 2003
TI Sustained-release compositions of estradiol metabolites and their derivatives
IN Allison, Dean S.; Schmidt, Paul G.; Hudnut, Paul S.
PA PR Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2003092585 | A2 | 20031113 | WO 2003-US12727 | 20030425 |
| | WO 2003092585 | A3 | 20040819 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,

NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRAI US 2002-377490P P 20020502
CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---|---|---|
| WO 2003092585 | ICM | A61K |

AB The present invention provides improved sustained-release formulations of estradiol metabolites, including 2-hydroxyestradiol, 2-methoxyestradiol, 4-hydroxyestradiol and 4-methoxyestradiol, useful for therapeutic treatments. The invention also provides methods of producing sustained-release forms of estradiol metabolites. The compns. of the present invention include microparticles, nanoparticles, patches, crystals, gels, rods, stints, pellets, disks, lozenges, wafers, capsules, films, microcapsules, nanocapsules, hydrogels, liposomes, implants and vaginal rings. Compns. also include formulations for transdermal and i.v. delivery of estradiol metabolites. The present invention provides numerous improvements over previous forms of estradiol metabolites, such advantages including the sustained release of normally short half-life compds. to maintain therapeutic blood levels. For example, 2-methoxyestradiol transdermal patch was prepared by suspending the drug in pressure-sensitive adhesives and coated onto polyethylene and aluminum vapor coated polyester backings.

ST estradiol metabolite deriv controlled release

IT Drug delivery systems
(capsules; sustained release compns. of estradiol metabolites and their derivs.)

IT Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(copolymer with orthoesters and urethanes; sustained release compns. of estradiol metabolites and their derivs.)

IT Drug delivery systems
(films; sustained release compns. of estradiol metabolites and their derivs.)

IT Drug delivery systems
(gels; sustained release compns. of estradiol metabolites and their derivs.)

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(glycolide-based; sustained release compns. of estradiol metabolites and their derivs.)

IT Drug delivery systems
(hydrogels; sustained release compns. of estradiol metabolites and their derivs.)

IT Drug delivery systems
(implants; sustained release compns. of estradiol metabolites and their derivs.)

IT Surfactants
(ionic; sustained release compns. of estradiol metabolites and their derivs.)

IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lactide; sustained release compns. of estradiol metabolites and their derivs.)

IT Drug delivery systems
(liposomes; sustained release compns. of estradiol metabolites and their derivs.)

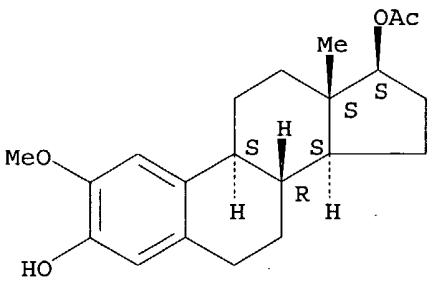
IT Drug delivery systems
(microcapsules; sustained release compns. of estradiol metabolites and their derivs.)

IT Drug delivery systems
(microparticles; sustained release compns. of estradiol metabolites and their derivs.)

IT Drug delivery systems
(microspheres; sustained release compns. of estradiol metabolites and their derivs.)
IT Drug delivery systems
(nanocapsules; sustained release compns. of estradiol metabolites and their derivs.)
IT Drug delivery systems
(nanoparticles; sustained release compns. of estradiol metabolites and their derivs.)
IT Drug delivery systems
(nasal; sustained release compns. of estradiol metabolites and their derivs.)
IT Surfactants
(nonionic; sustained release compns. of estradiol metabolites and their derivs.)
IT Drug delivery systems
(ophthalmic; sustained release compns. of estradiol metabolites and their derivs.)
IT Drug delivery systems
(oral; sustained release compns. of estradiol metabolites and their derivs.)
IT Polyethers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ortho ester group-containing; sustained release compns. of estradiol metabolites and their derivs.)
IT Drug delivery systems
(pellets; sustained release compns. of estradiol metabolites and their derivs.)
IT Polyamides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(poly(amino acids); sustained release compns. of estradiol metabolites and their derivs.)
IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyamide-; sustained release compns. of estradiol metabolites and their derivs.)
IT Polyamides, biological studies
Polyethers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyester-; sustained release compns. of estradiol metabolites and their derivs.)
IT Polyesters, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(polyether-; sustained release compns. of estradiol metabolites and their derivs.)
IT Drug delivery systems
(prodrugs; sustained release compns. of estradiol metabolites and their derivs.)
IT Antioxidants
Buffers
Encapsulation
(sustained release compns. of estradiol metabolites and their derivs.)
IT Lecithins
Peptides, biological studies
Phospholipids, biological studies
Polyanhydrides
Polycarbonates, biological studies
Polymer blends
Polyoxyalkylenes, biological studies
Polyurethanes, biological studies
Tocopherols
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sustained release compns. of estradiol metabolites and their derivs.)

IT Drug delivery systems
(sustained-release; sustained release compns. of estradiol metabolites and their derivs.)
IT Drug delivery systems
(tapes, buccal; sustained release compns. of estradiol metabolites and their derivs.)
IT Drug delivery systems
(transdermal; sustained release compns. of estradiol metabolites and their derivs.)
IT Drug delivery systems
(vaginal; sustained release compns. of estradiol metabolites and their derivs.)
IT 106392-12-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Poloxamer; sustained release compns. of estradiol metabolites and their derivs.)
IT 50-28-2D, Estradiol, metabolite, derivs. 121-79-9, Propyl gallate 128-37-0, Butylated hydroxytoluene, biological studies 137-66-6, Ascorbyl palmitate 362-05-0, 2-Hydroxyestradiol 362-07-2, 2-Methoxyestradiol 5976-61-4, 4-Hydroxyestradiol 7002-78-0 7291-56-7 7291-57-8 9002-89-5, Polyvinyl alcohol 9003-39-8, Polyvinyl pyrrolidone 15802-18-3D, Cyanoacrylic acid, esters, polymers 23463-05-0 24980-41-4, Polycaprolactone 25248-42-4, Polycaprolactone 25322-68-3, Poly(ethylene glycol) 25322-68-3D, Polyethylene glycol, copolymer with orthoesters and urethanes 25322-69-4, Poly(Propylene glycol) 26009-03-0, Poly(glycolic acid) 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Poly(lactic acid) 26124-68-5, Poly(glycolic acid) 26780-50-7, Poly(lactide-co-glycolide) 26780-50-7D, Poly(lactide-co-glycolide), derivs. 26788-23-8, 4-Methoxyestradiol 31621-87-1, Poly(dioxanone) 34346-01-5, Poly(glycolic acid-lactic acid) 37492-86-7 **52717-98-3** 79787-03-4 79795-26-9 83187-96-6 83274-89-9 84509-93-3 111162-54-0 111162-55-1 111162-82-4 144082-85-9 144082-86-0 622839-99-0 622840-00-0 622840-01-1 622840-02-2 622840-03-3 622840-04-4 622840-05-5 622840-06-6 622840-07-7 622840-08-8 622840-09-9 622840-10-2 622840-11-3 622840-12-4 622840-13-5 622840-14-6 622840-15-7 622840-16-8 622840-17-9 622840-32-8
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sustained release compns. of estradiol metabolites and their derivs.)
IT **52717-98-3**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sustained release compns. of estradiol metabolites and their derivs.)
RN 52717-98-3 HCAPLUS
CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, 17-acetate, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




L31 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:888569 HCAPLUS

DN 137:370278
ED Entered STN: 22 Nov 2002
TI Preparation of substituted pregna-1,3,5(10)-triene derivatives for pharmaceutical use
IN Hesse, Robert Henry; Setty, Sundara Katugam Srinivasasetty; Pechet, Maurice Murdoch; Gile, Michael
PA Marsden, John Christopher, UK; Research Institute for Medicine and Chemistry Inc.
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-56
ICS A61K031-575; C07J041-00; A61P035-00
CC 32-5 (Steroids)
Section cross-reference(s): 1, 2, 63
FAN.CNT 1

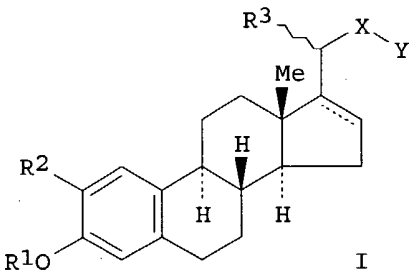
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2002092100 | A1 | 20021121 | WO 2002-GB2210 | 20020513 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2001-290013P P 20010511
CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---|---|---|
| WO 2002092100 | ICM | A61K031-56 |
| | ICS | A61K031-575; C07J041-00; A61P035-00 |

OS MARPAT 137:370278
GI



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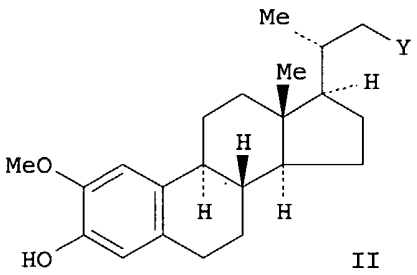


II

AB Pregna-1,3,5(10)-triene derivs., such as I [R1 = H, hydroxy protecting group; R2 = OH, CHO, alkoxy, alkenyl, alkyl, etc.; R3 = α-, β-Me; X = C1-3 alkylene group, bond; Y = C(R4)(R5)NR6R7; R4, R5 = H, alkyl, alkenyl and alkynyl groups, such that the total carbon content of R4 and R5 does not exceed three atoms; R6 = H, aliphatic or aràliph. organic group, acyl, etc.; C16-C17 = saturated, unsatd.], were prepared for a variety of therapeutic uses, such as modulating cell activity, including

antiproliferative and antiangiogenic effects. Thus, pregna-1,3,5(10)-triene derivs. II (Y = NH2, NHCOMe) were prepared via a multistep synthetic series starting from 2-methoxy-3-[[tris(1-methylethyl)silyl]oxy]-estra-1,3,5(10)-trien-17-one and ethyltriphenylphosphonium bromide. Pharmaceutical compns. of the prepared compds. were discussed, but specific pharmaceutical activity testing data was not presented.

ST norpregnatriene prepn antiproliferative antiangiogenic agent

IT Mental disorder
(cognitive, treatment; preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT Blood coagulation
Cognition
(disorder, treatment; preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT Transplant and Transplantation
(graft-vs.-host reaction, treatment; preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT Anti-inflammatory agents
Anticholesteremic agents
Antitumor agents
Cognition enhancers
Contraceptives
Immunomodulators
(preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT Arthritis
(psoriatic arthritis, treatment; preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT Mental disorder
(senile psychosis, treatment; preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT Asthma
Autoimmune disease
Bone, disease
Hypercholesterolemia
Hyperplasia
Hypertension
Inflammation
Neoplasm
Rheumatoid arthritis
Skin, disease
Transplant rejection
(treatment; preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT 4736-60-1, Ethyltriphenylphosphonium iodide 305812-67-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT **229486-17-3P** 305812-87-7P 305812-99-1P 372952-47-1P
372952-49-3P 372952-50-6P 475486-81-8P 475486-82-9P 475486-83-0P
475486-84-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

IT 475486-79-4P 475486-80-7P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)

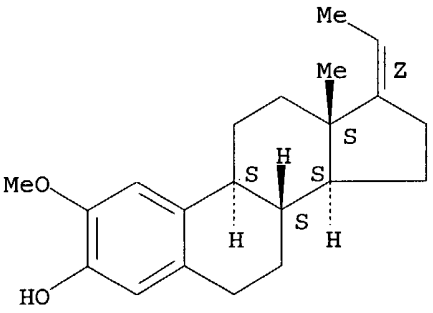
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Christopher, M; WO 0068246 A 2000 HCAPLUS

(2) Christopher, M; WO 0185755 A 2001 HCAPLUS
(3) Cushman, M; JOURNAL OF MEDICINAL CHEMISTRY 1995, V38(12), P2041 HCAPLUS
(4) Jacques, P; US 3291690 A 1966
IT **229486-17-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted pregna-1,3,5(10)-triene derivs. for a variety of therapeutic uses)
RN 229486-17-3 HCAPLUS
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.




L31 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:833342 HCAPLUS
DN 135:358085
ED Entered STN: 16 Nov 2001
TI Preparation of 2-substituted pregna-1,3,5(10)-triene and chola-1,3,5(10)-triene derivatives with antiproliferative and antiangiogenic activity
IN Hesse, Robert Henry; Setty, Sundara Katugam Srinivasasetty; Pechet, Maurice Murdoch; Gile, Michael
PA Marsden, John Christopher, UK; Research Institute for Medicine and Chemistry Inc.
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07J041-00
ICS A61K031-57; C07J009-00; C07J013-00; C07J051-00; A61K031-575; A61P005-30; A61P035-00
CC 32-5 (Steroids)
Section cross-reference(s): 1, 63
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2001085755 | A1 | 20011115 | WO 2001-GB2103 | 20010511 |

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

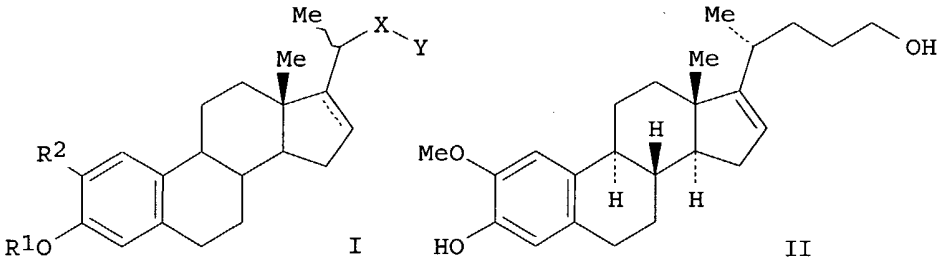
| | | | | | |
|---|---|---|---|---|---|
| | EP 1287017 | A1 | 20030305 | EP 2001-928120 | 20010511 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| | JP 2003532737 | T2 | 20031105 | JP 2001-582354 | 20010511 |
| | NZ 523042 | A | 20040528 | NZ 2001-523042 | 20010511 |
| | ZA 2002009060 | A | 20040209 | ZA 2002-9060 | 20021107 |
| | NO 2002005392 | A | 20030109 | NO 2002-5392 | 20021111 |
| | US 2003158167 | A1 | 20030821 | US 2003-275257 | 20030313 |
| PRAI | US 2000-203462P | P | 20000511 | | |
| | WO 2001-GB2103 | W | 20010511 | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---|---|---|
| WO 2001085755 | ICM | C07J041-00 |
| | ICS | A61K031-57; C07J009-00; C07J013-00; C07J051-00; A61K031-575; A61P005-30; A61P035-00 |

OS MARPAT 135:358085

GI




AB Compds. of formula I [R1 = H, protecting group; R2 = OH, alkoxy, CHO, alkenyl, etc.; X = alkylene, bond; Y = CHO, (substituted) CH2OH, etc.] are prepared which exhibit potent cell modulating activity, including antiproliferative and antiangiogenic effects. Thus, 2-methoxy-3-triisopropylsilyloxy-19-norpregn-1,3,5(10),17(20)Z-tetraene (preparation given) is reacted with Me acrylate, reduced with LiAlH4, and desilylated with TBAF to give II.

ST pregnatriene deriv prepn antiproliferative antiangiogenic; cholatriene deriv prepn antiproliferative antiangiogenic; antiproliferative pregnatriene cholatriene deriv; antiangiogenic pregnatriene cholatriene deriv

IT Angiogenesis inhibitors
Antitumor agents
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT Proliferation inhibition
(proliferation inhibitors; preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT 372952-25-5P 372952-27-7P 372952-29-9P 372952-30-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT 372952-23-3P 372952-24-4P 372952-28-8P 372952-31-3P 372952-32-4P
372952-33-5P 372952-34-6P 372952-35-7P 372952-36-8P 372952-37-9P
372952-38-0P 372952-39-1P 372952-40-4P 372952-41-5P 372952-42-6P
372952-43-7P 372952-44-8P 372952-45-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT 96-33-3, Methyl acrylate 305812-67-3 372952-58-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

IT **229486-17-3P** 305812-87-7P 305812-89-9P 305812-91-3P
305812-97-9P 372952-46-0P 372952-47-1P 372952-48-2P 372952-49-3P
372952-50-6P 372952-51-7P 372952-52-8P 372952-53-9P 372952-54-0P
372952-55-1P 372952-56-2P 372952-57-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

RE.CNT 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD

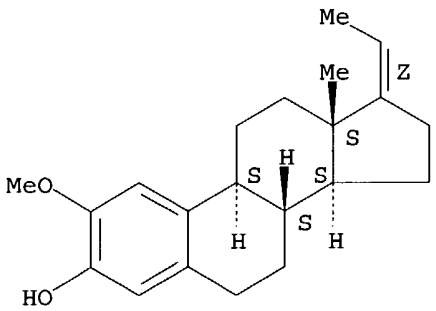
RE

(1) Cushman, M; JOURNAL OF MEDICINAL CHEMISTRY 1995, V38(12), P2041 HCAPLUS
(2) Marsden, J; WO 0068246 A 2000 HCAPLUS
(3) Mitsubishi Chemical Industries Co Ltd; JP 54112849 A HCAPLUS
(4) Mitsubishi Chemical Industries Co Ltd; JP 54112850 A HCAPLUS
(5) Mitsubishi Chemical Industries Co Ltd; JP 54117454 A HCAPLUS
(6) Mitsubishi Chemical Industries Co Ltd; JP 54117455 A HCAPLUS
(7) Mitsubishi Chemical Industries Co Ltd; JP 54117456 A HCAPLUS
(8) Mitsubishi Chemical Industries Co Ltd; JP 54112849 A 1979 HCAPLUS
(9) Mitsubishi Chemical Industries Co Ltd; JP 54112850 A 1979 HCAPLUS
(10) Mitsubishi Chemical Industries Co Ltd; JP 54117454 A 1979 HCAPLUS
(11) Mitsubishi Chemical Industries Co Ltd; JP 54117455 A 1979 HCAPLUS
(12) Mitsubishi Chemical Industries Co Ltd; JP 54117456 A 1979 HCAPLUS
(13) Mitsubishi Chemical Industries Co Ltd; PATENT ABSTRACTS OF JAPAN 1979, V003(133), PC-063
(14) Mitsubishi Chemical Industries Co Ltd; PATENT ABSTRACTS OF JAPAN 1979, V003(133), PC-063
(15) Ruggieri, P; US 3562260 A 1971 HCAPLUS

IT **229486-17-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)

RN 229486-17-3 HCAPLUS
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.




L31 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:283974 HCAPLUS
DN 134:295993

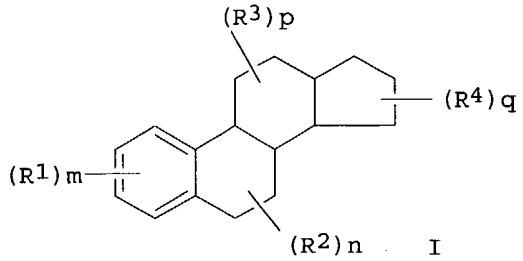
ED Entered STN: 20 Apr 2001
TI Estradiol conjugates and their therapeutic applications
IN Stewart, Alastair George; McAllister, David James; Collis, Maree Patricia; Robertson, Alan Duncan
PA University of Melbourne, Australia
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07J001-00
ICS A61K047-36; A61K047-42; A61K047-48; A61P009-00; A61P035-00
CC 32-3 (Steroids)
Section cross-reference(s): 1, 2, 33
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2001027132 | A1 | 20010419 | WO 2000-AU1244 | 20001013 |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | EP 1226154 | A1 | 20020731 | EP 2000-969105 | 20001013 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| | JP 2003511461 | T2 | 20030325 | JP 2001-530350 | 20001013 |
| | ZA 2002002622 | A | 20030304 | ZA 2002-2622 | 20020404 |
| PRAI | AU 1999-3425 | A | 19991014 | | |
| | WO 2000-AU1244 | W | 20001013 | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---|---|---|
| WO 2001027132 | ICM | C07J001-00 |
| | ICS | A61K047-36; A61K047-42; A61K047-48; A61P009-00; A61P035-00 |

OS MARPAT 134:295993
GI

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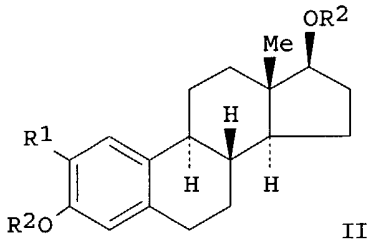



II

AB The invention discloses the preparation of conjugated prodrug of estradiol compound I (R1-R4 = H, OH, halo, alkyl, alkenyl, alkynyl, cycloalkyl, amino, aryl, keto, hydrazono, oximino, carbohydrate, peptide, etc.; m,n,p,q = 0-3), a pharmaceutically acceptable salt or in vivo hydrolyzable ester, amide carbonate or carbamate thereof, in the treatment of conditions associated with enhanced angiogenesis or accelerated cell division, such as cancer, and inflammatory conditions such as asthma and rheumatoid

arthritis and hyperproliferative skin disorders including psoriasis. Thus, II [R1 = OMe, R2 = H (III)] was prepared via multi-step reaction sequence starting from β-estradiol II (R1-R2 = H). In human airway fibroblasts thrombin-stimulated increases in cell number were reduced to 12 ± 8% of the control response by III.

ST estradiol conjugate prodrug prepn angiogenesis inhibitor

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(conjugates; preparation of peptide conjugated prodrug of estradiol compds. for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

IT Partition
(for the measurement of relative solubilities of estradiol conjugates)

IT Glycosides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(glucuronides, estrogenic; preparation of glucuronide prodrug of estradiol compds. for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

IT Estrogens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(hydroxy, glucuronides; preparation of glucuronide prodrug of estradiol compds. for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

IT Fluorometry
(in determination of relative solubilities of estradiol conjugates for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

IT Antitumor agents
(preparation of conjugated prodrug of estradiol compds. for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

IT Antiasthmatics
Rheumatoid arthritis
(preparation of conjugated prodrug of estradiol compds. for the treatment of inflammatory conditions such as asthma and rheumatoid arthritis)

IT Psoriasis
(preparation of conjugated prodrug of estradiol compds. for the treatment psoriasis)

IT Estrogen receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of estradiol conjugates and their binding with rat uterine cytosol estrogen receptor)

IT DNA formation
(preparation of estradiol conjugates for regulation of DNA synthesis)

IT Respiratory tract
(preparation of estradiol conjugates for regulation of airway mesenchymal cell number)

IT Angiogenesis inhibitors
Anti-inflammatory agents
(preparation of estradiol conjugates for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

IT Estrogens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of estradiol conjugates for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

IT Galactosides
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of galactoside prodrug of estradiol compds. for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

IT Drug delivery systems
(prodrugs; preparation of conjugated prodrug of an estradiol compds. for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

IT Proliferation inhibition
(proliferation inhibitors; preparation of estradiol conjugates for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

IT Skin, disease
(proliferative; preparation of conjugated prodrug of estradiol compds. for the treatment of hyperproliferative skin disorders)

IT 7291-57-8P 69540-62-1P 334791-42-3P 334791-45-6P 334791-46-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of estradiol conjugates for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

IT 171064-21-4P 334791-43-4P 334791-47-8P 334791-49-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of estradiol conjugates for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

IT 9001-45-0, β-Glucuronidase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of estradiol conjugates for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

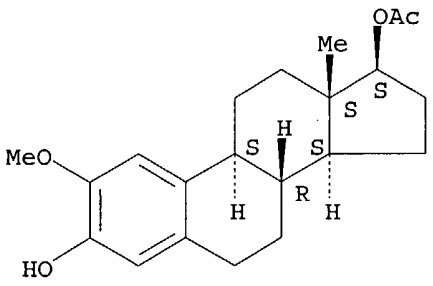
IT **52717-98-3P**
RL: BYP (Byproduct); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of estradiol conjugates for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

IT 513-78-0, Cadmium carbonate
RL: CAT (Catalyst use); USES (Uses)
(preparation of estradiol conjugates for the treatment of conditions associated with enhanced angiogenesis or accelerated cell division)

IT 50-28-2, β-Estradiol, reactions 100-39-0, Benzyl bromide 108-24-7, Acetic anhydride 3068-32-4 7803-57-8, Hydrazine hydrate 21085-72-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of estradiol conjugates for the treatment of conditions associated

with enhanced angiogenesis or accelerated cell division)
IT 362-07-2P 69455-04-5P 69540-63-2P 83274-89-9P 159143-75-6P
159143-76-7P 192062-05-8P 334791-44-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of estradiol conjugates for the treatment of conditions associated
with enhanced angiogenesis or accelerated cell division)
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Berg, D; Hoppe-Seyler's Z Physiol Chem 1982, V363(7), P737 HCAPLUS
(2) Holler, M; Acta Endocrinologica 1982, V100, P57 MEDLINE
(3) Nakagawa, A; Chem Pharm Bull 1978, V26(11), P3567 HCAPLUS
(4) Nambara, T; Chem Pharm Bull 1976, V24(3), P421 HCAPLUS
(5) Nambara, T; Chem Pharm Bull 1977, V25(5), P942 HCAPLUS
(6) Ohkubo, T; Steroids 1990, V55(3), P128 HCAPLUS
(7) Rohle, G; Hoppe-Seyler's Z Physiol Chem 1974, V355, P490 MEDLINE
(8) Spiegelhalder, B; Journal of Steroid Biochemistry 1976, V7, P749 HCAPLUS
(9) Stalford, A; Steroids 1997, V62, P750 HCAPLUS
(10) Takanashi, K; Bunseki Kagaku 1995, V44(10), P793 HCAPLUS
(11) The Children'S Medical Center Corporation; WO 9504535 1995 HCAPLUS
(12) Watanabe, K; Chem Pharm Bull 1982, V30(9), P3231 HCAPLUS
IT **52717-98-3P**
RL: BYP (Byproduct); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of estradiol conjugates for the treatment of conditions associated
with enhanced angiogenesis or accelerated cell division)
RN 52717-98-3 HCAPLUS
CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, 17-acetate, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




L31 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:814500 HCAPLUS
DN 133:350395
ED Entered STN: 21 Nov 2000
TI Synthesis of cholestane compounds with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy
IN Hesse, Robert Henry; Setty, Sundara Katugam Srinivasasetty; Ramgopal, Malathi; Kugabalusooriar, Sanga
PA Marsden, John, Christopher, UK; Research Institute for Medicine and Chemistry Inc.
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07J009-00
ICS C07J041-00; A61K031-575; C07J051-00; A61P017-02; A61P019-08;

A61P037-06; A61P029-00; A61P035-00; A61P021-00; A61P009-10;
A61P005-20; A61P017-00; A61P009-12; A61P019-02; A61P011-06;
A61P025-28; A61P015-18; A61P007-02; A61P003-06

CC 32-7 (Steroids)
Section cross-reference(s): 1, 2

FAN.CNT 1

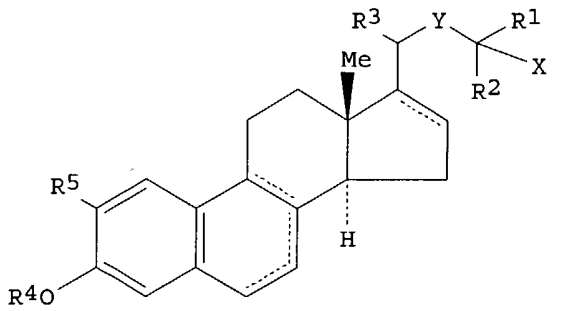
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2000068246 | A1 | 20001116 | WO 2000-GB1813 | 20000511 |
| W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1179005 | A1 | 20020213 | EP 2000-927569 | 20000511 |
| EP 1179005 | B1 | 20031119 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| AT 254629 | E | 20031215 | AT 2000-927569 | 20000511 |
| PT 1179005 | T | 20040430 | PT 2000-927569 | 20000511 |
| NZ 515482 | A | 20040528 | NZ 2000-515482 | 20000511 |
| ES 2207509 | T3 | 20040601 | ES 2000-927569 | 20000511 |
| ZA 2001009272 | A | 20021128 | ZA 2001-9272 | 20011109 |
| NO 2001005520 | A | 20020109 | NO 2001-5520 | 20011112 |
| PRAI GB 1999-10934 | A | 19990511 | | |
| WO 2000-GB1813 | W | 20000511 | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---|---|---|
| WO 2000068246 | ICM | C07J009-00 |
| | ICS | C07J041-00; A61K031-575; C07J051-00; A61P017-02; A61P019-08; A61P037-06; A61P029-00; A61P035-00; A61P021-00; A61P009-10; A61P005-20; A61P017-00; A61P009-12; A61P019-02; A61P011-06; A61P025-28; A61P015-18; A61P007-02; A61P003-06 |

OS MARPAT 133:350395

GI




I

AB Synthesis of cholestane compds. (I) [R1 and R2, which may be the same or different, = alkyl, alkenyl, alkynyl; R3 = Me having α- or β-configuration; R4 = H or an etherifying or esterifying group; R5 = H, OH, alkoxy; X = OR4, wherein R4 is as defined above, or NR6R7 wherein R6 = H, aliphatic or araliph. organic group, acyl group comprising aliphatic,

araliph. or aryl organic group linked to the nitrogen atom by way of a carbonyl group; R7 = H, alkyl; Y = (un)substituted alkylene, alkenylene, alkynylene; dotted lines signify that double bonds may be present at the 16(17)-position and/or either at the 6(7)- and 8(9)-positions or at the 7(8)-position] is disclosed for modulation of cell growth and differentiation, while having low calcemic activity. Thus, I [R1,R2 = Me; R3 = α-Me; R4,R5 = H; X = NHAc; Y = (CH2)4; Δ16 double bond] is prepared by reaction of 3-triisopropylsilyloxy-19-norchol-1,3,5(10),16-tetraene-24-bromide with acetoniltrile followed by reduction of nitrile to amine, methylation of amine with Me lithium, acetylation of the amino with acetic anhydride and desilylation with TBAF.

ST cholestane analog prepn cell growth modulation differentiation; low calcemic activity cholestane analog

IT Steroids, preparation
Steroids, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aromatic; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Transplant and Transplantation
(host-vs.-graft reaction; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Arthritis
(psoriatic arthritis; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Hyperparathyroidism
(secondary; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Mental disorder
(senile psychosis; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Heart, disease
(spondylitic; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Aromatic hydrocarbons, preparation
Aromatic hydrocarbons, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(steroids; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT Anti-inflammatory agents
Antitumor agents
Asthma
Autoimmune disease
Blood coagulation
Bone, disease
Burn
Fertility
Hyperplasia
Hypertension
Intestine, disease
Muscle, disease
Rheumatoid arthritis
Skin, disease
Transplant rejection
Wound healing
(synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT 57-88-5, Cholest-5-en-3-ol (3β)-, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(blood reduction; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT 9002-64-6, Parathyroid hormone
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(suppression; synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT 305812-17-3P 305812-18-4P 305812-52-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT 305812-19-5P 305812-20-8P 305812-21-9P 305812-22-0P 305812-23-1P
305812-24-2P 305812-25-3P 305812-26-4P 305812-27-5P 305812-28-6P
305812-29-7P 305812-30-0P 305812-31-1P 305812-32-2P 305812-33-3P
305812-34-4P 305812-35-5P 305812-36-6P 305812-37-7P 305812-38-8P
305812-39-9P 305812-40-2P 305812-41-3P 305812-42-4P 305812-43-5P
305812-44-6P 305812-45-7P 305812-46-8P 305812-47-9P 305812-48-0P
305812-49-1P 305812-50-4P 305812-51-5P 305812-53-7P 305812-54-8P
305812-55-9P 305812-56-0P 305812-57-1P 305812-58-2P 305812-59-3P
305812-60-6P 305812-61-7P 305812-62-8P 305812-63-9P 305812-64-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

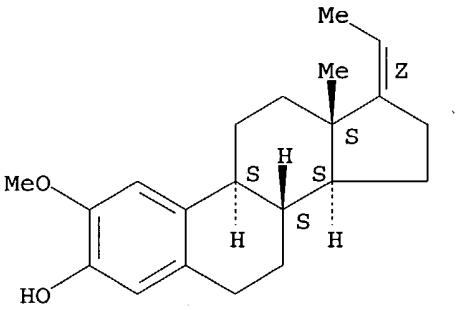
IT 74-88-4, Methyl iodide, reactions 75-03-6, Ethyl iodide 75-05-8, Acetonitrile, reactions 78-77-3, Isobutyl bromide 96-33-3 98-88-4, Benzoyl chloride 103-80-0, Phenylacetyl chloride 106-96-7, Propargyl bromide 474-87-3 517-09-9 867-13-0 922-67-8, Methyl propiolate 1439-36-7, 1-Triphenylphosphoranylidene-2-propanone 3234-64-8, 1,1-Diethylpropargylamine 4736-60-1, Ethyl triphenylphosphonium iodide 7103-48-2, Estrone-3-tetrahydropyranyl ether 17963-41-6 305812-65-1 305812-66-2 305812-67-3 305812-69-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

IT **229486-17-3P** 305812-70-8P 305812-71-9P 305812-72-0P
305812-73-1P 305812-75-3P 305812-76-4P 305812-77-5P 305812-79-7P
305812-81-1P 305812-83-3P 305812-85-5P 305812-87-7P 305812-89-9P
305812-91-3P 305812-93-5P 305812-95-7P 305812-97-9P 305812-99-1P
305813-01-8P 305813-03-0P 305813-05-2P 305813-07-4P 305813-09-6P
305813-10-9P 305813-12-1P 305813-14-3P 305813-15-4P 305813-16-5P
305813-17-6P 305813-19-8P 305813-20-1P 305813-21-2P 305813-22-3P
305813-23-4P 305813-25-6P 305813-26-7P 305813-27-8P 305813-28-9P
305813-30-3P 305813-32-5P 305813-34-7P 305813-36-9P 305813-38-1P
305813-39-2P 305813-40-5P 305813-41-6P 305813-42-7P 305813-43-8P
305813-44-9P 305813-45-0P 305813-46-1P 305813-47-2P 305813-48-3P
305813-49-4P 305813-50-7P 305813-51-8P 305813-52-9P 305813-53-0P
305813-54-1P 305813-55-2P 305813-56-3P 305813-57-4P 305813-58-5P
305813-59-6P 305813-60-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Escaleira; 1993, 7, HCAPLUS
(2) Escaleira; J STEROID BIOCHEM MOL BIOL 1993, V45(4), P257 HCAPLUS
(3) Laing, S; US 3717627 A 1973
(4) Lajeunesse; 1994, 23, HCAPLUS
(5) Lajeunesse; BONE MINER 1994, V24(1), P1 HCAPLUS

(6) Liel; 1992, 25, HCAPLUS
(7) Liel; ENDOCRINOLOGY (BALTIMORE) 1992, V130(5), P2597 HCAPLUS
(8) Mountford; 1999, 8, HCAPLUS
(9) Mountford; EXP HEMATOL (N Y) 1999, V27(3), P451 HCAPLUS
(10) Ruggieri, P; US 3562260 A 1971 HCAPLUS
IT **229486-17-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of cholestane compds. with a c17-alkyl side chain and an aromatic A-ring for use in cell modulating therapy)
RN 229486-17-3 HCAPLUS
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.




L31 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:460438 HCAPLUS
DN 131:88083
ED Entered STN: 28 Jul 1999
TI Preparation of estrone sulfamate inhibitors of estrone sulfatase
IN Tanabe, Masato; Peters, Richard H.; Chao, Wan-Ru; Shigeno, Kazuhiko
PA SRI International, USA
SO PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07J041-00
ICS A61K031-565; A61K031-57; A61K031-575
CC 32-3 (Steroids)
Section cross-reference(s): 2, 63
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9933858 | A2 | 19990708 | WO 1998-US27333 | 19981221 |
| | W: AU, CA, JP, KR | | | | |
| | RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| | US 6046186 | A | 20000404 | US 1997-997416 | 19971224 |
| | CA 2318349 | AA | 19990708 | CA 1998-2318349 | 19981221 |
| | AU 9919416 | A1 | 19990719 | AU 1999-19416 | 19981221 |
| | AU 751732 | B2 | 20020829 | | |
| | EP 1042354 | A2 | 20001011 | EP 1998-964243 | 19981221 |
| | EP 1042354 | B1 | 20040303 | | |
| | R: DE, FR, GB, IT, NL | | | | |
| | JP 2001527089 | T2 | 20011225 | JP 2000-526534 | 19981221 |
| | EP 1405860 | A1 | 20040407 | EP 2003-28361 | 19981221 |
| | R: DE, FR, GB, IT, NL | | | | |

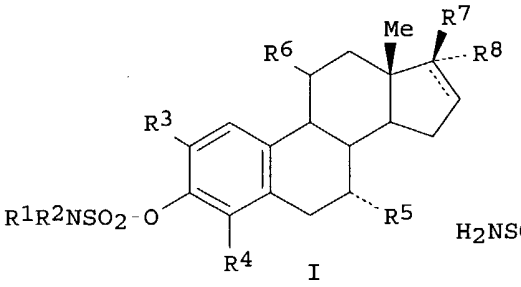
PRAI US 1997-997416 A 19971224
EP 1998-964243 A3 19981221
WO 1998-US27333 W 19981221

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---|---|---|
| WO 9933858 | ICM | C07J041-00 |
| | ICS | A61K031-565; A61K031-57; A61K031-575 |
| WO 9933858 | ECLA | C07J041/00B; C07J041/00C40; C07J041/00C70 |
| US 6046186 | ECLA | C07J041/00B; C07J041/00C40; C07J041/00C70 |
| EP 1405860 | ECLA | C07J041/00B; C07J041/00C40; C07J041/00C70 |

OS MARPAT 131:88083

GI

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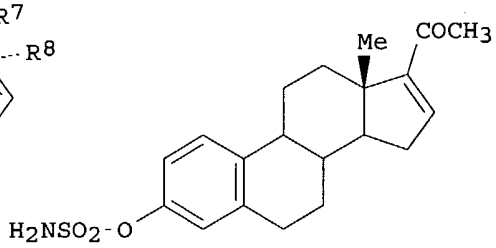



II

AB Novel compds.of formula I [R1, R2 = H, alkyl, etc.; R3 = H, CN, NO2, COOH, alkoxycarbonyl, etc.; R4 = H, NO2, (substituted) amino; R5, R6 = H, alkyl; R7, R8 = H, alkyl, alkenyl, alkynyl, alkoxy, acyl, acyloxy, etc.; R7,R8 = oxo, alkylidene, etc.] are prepared as inhibitors of estrone sulfatase. Thus, II is prepared from ethynylestradiol in 4 steps. and showed estrone sulfatase inhibitory activity of IC50 = 21 pM. Pharmaceutical compns. and methods for using I to treat estrogen-dependent disorders are provided.

ST estrone sulfamate prepn estrone sulfatase inhibitor

IT Estrogens
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antiestrogens; preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT Antitumor agents
(preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT 59298-96-3, Estrone sulfatase
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibitors; preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT 185910-34-3P 185910-42-3P 208924-86-1P 208924-87-2P 229485-78-3P
229485-79-4P 229485-80-7P 229485-81-8P 229485-82-9P 229485-83-0P
229485-84-1P 229485-85-2P 229485-86-3P 229485-87-4P 229485-88-5P
229485-89-6P 229485-90-9P 229485-91-0P 229485-92-1P 229485-93-2P
229485-94-3P 229485-95-4P 229485-96-5P 229485-97-6P 229485-98-7P
229485-99-8P 229486-00-4P 229486-01-5P 229486-02-6P 229486-03-7P
229486-04-8P 229486-05-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT 50-28-2, Estradiol, reactions 53-16-7, Estrone, reactions 57-63-6, Ethynylestradiol 108-01-0, N,N-Dimethylethanolamine 109-77-3, Malononitrile 362-08-3 867-13-0, Triethylphosphonoacetate 1779-51-7,

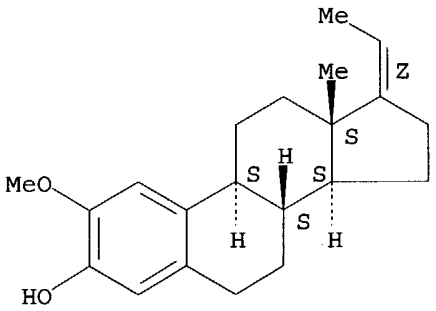
Butyltriphenylphosphonium bromide 4584-46-7 5407-04-5 6228-47-3,
Propyltriphenylphosphonium bromide 7678-95-7 67530-18-1 229486-27-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT 858-98-0P 1667-98-7P 4736-62-3P 5774-17-4P 5779-47-5P 5976-73-8P
5976-74-9P 6599-97-9P 13879-55-5P 13879-57-7P 14030-45-6P
14846-63-0P 14982-15-1P 15001-40-8P 22787-09-3P 23880-59-3P
31559-52-1P 57711-40-7P 59077-04-2P, 19-Norpregna-1,3,5(10)-trien-3-ol
59452-15-2P 59452-16-3P, 19,21-Dinorchola-1,3,5(10)-trien-3-ol
64215-82-3P 67519-62-4P 71716-18-2P 96111-26-1P 101766-63-6P
115208-23-6P 115387-92-3P 116627-15-7P 116627-20-4P 120574-27-8P
120574-28-9P 165619-18-1P 165619-19-2P 165619-20-5P 185910-40-1P
206442-55-9P 208758-44-5P 208758-45-6P 208758-46-7P 208758-49-0P
208758-50-3P 229486-06-0P 229486-07-1P 229486-08-2P 229486-09-3P
229486-10-6P 229486-11-7P 229486-12-8P 229486-13-9P 229486-14-0P
229486-15-1P 229486-16-2P **229486-17-3P 229486-18-4P**
229486-19-5P 229486-20-8P 229486-21-9P 229486-22-0P 229486-23-1P
229486-24-2P 229486-25-3P 229486-26-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of estrone sulfamates as inhibitors of estrone sulfatase)

IT **229486-17-3P 229486-18-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of estrone sulfamates as inhibitors of estrone sulfatase)

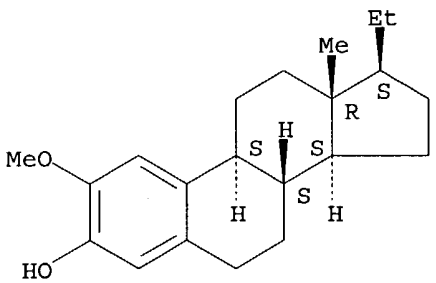
RN 229486-17-3 HCAPLUS
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

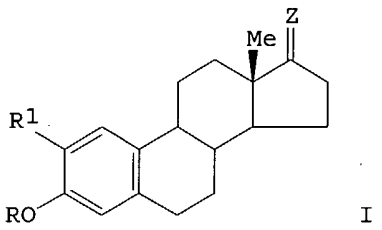



RN 229486-18-4 HCAPLUS
CN 19-Norpregna-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1978:121515 HCAPLUS
DN 88:121515
ED Entered STN: 12 May 1984
TI Synthesis of 2-methoxy-17α-ethynylestradiol and its 3-methyl ether. The Loudon ortho-hydroxylation reaction
AU Ei, Kei-Hwie; Teng, Ying-Hsiang; Wang, Wen-Jong; Chao, Hwa-Ming; Hsu, Zhen-Pon
CS Szechwan Univ., Chengtu, Peop. Rep. China
SO Kexue Tongbao (Chinese Edition) (1977), 22(12), 539-42
CODEN: KHTPAT; ISSN: 0023-074X
DT Journal
LA Chinese
CC 32-3 (Steroids)
GI

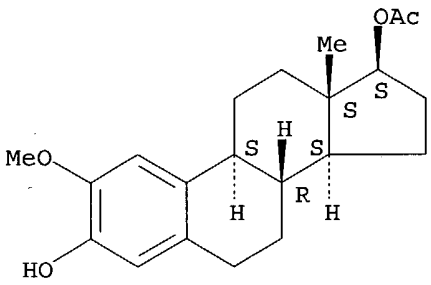



I

AB Title estradiol (I, R = H, R1 = MeO, Z = α-C.tplbond.CH, β-OH) (II) was prepared by hydroxylation of I [R = 2,5-(PhCO)(O2N)C6H3, R1 = H, Z = α-H, β-OAc] (obtained by heating 17β-estradiol with 2,5-Cl(O2N)C6H3COPh followed by acetylation) with HOAc-concentrated H2SO4 and then H2O2 and subsequent 2-O-methylation, hydrolysis, Jones oxidation, reduction, and ethynylation using of KC.tplbond.CH. 3-O-methylation of II with CH2N2 gave I (R = Me, R1 = MeO, Z = α-C.tplbond.CH, β-OH).
ST ethynylmethoxyestradiol; Loudon hydroxylation estradiol; estradiol ethynyl ethoxy methyl; steroid hydroxy unsatd
IT Steroids, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(17β-hydroxy-1,3,5-unsatd., preparation of, Loudon hydroxylation for)
IT Hydroxylation
(Loudon, of estradiol)
IT 26011-40-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(methylation of)
IT 65932-52-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and Jones oxidation of)
IT 65932-49-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acetylation of)
IT 53-16-7P, preparation
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and ethynylation of)
IT 65932-51-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)
IT 22415-44-7P 38781-50-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and methylation of)
IT 65932-50-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and oxidation of)
IT 65932-53-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reduction of)
IT 362-07-2P **52717-98-3P** 55236-35-6P 65975-87-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
IT 50-28-2, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with 2-chloro-5-nitrobenzophenone)
IT 34052-37-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with estradiol)
IT **52717-98-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 52717-98-3 HCAPLUS
CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, 17-acetate, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




L31 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1974:404163 HCAPLUS
DN 81:4163
ED Entered STN: 12 May 1984
TI Synthesis of glucuronides of 2-hydroxylated estrogens and their methyl ethers
AU Roehle, Gerhard; Breuer, Heinz
CS Inst. Klin. Biochem., Bonn, Fed. Rep. Ger.
SO Hoppe-Seyler's Zeitschrift fuer Physiologische Chemie (1974), 355(4), 490-4
CODEN: HSZPAZ; ISSN: 0018-4888
DT Journal
LA English
CC 33-3 (Carbohydrates)
Section cross-reference(s): 32
AB The chemical synthesis of the phenolic β-D-glucuronides of 2-methoxy-17β-estradiol, 2-hydroxy-17β-estradiol (I) and its 3-Me ether was described. Thus, reaction of the 17-acetate of I with Me 2,3,4-tri-O-acetyl-1-bromo-1-deoxy-α-D-glucopyranuronate in the presence of Cd carbonate gave only the corresponding 2-glucuronide. Under the exptl. conditions employed, no 3-glucuronide was formed. The

selectivity of the glucuronidation reaction is not in accord. with the suggestion, made by J. Fishman et al. (1967), that thephenolic groups in ring A of 2-hydroxy estrogens may be chemical indistinguishable.

ST hydroxyestrogen glucuronidation; estrogen hydroxy glucuronidation

IT Steroids, preparation
RL: PREP (Preparation)
(hydroxyestradiol glucuronides)

IT 27736-75-0P 52718-00-0P 52718-01-1P 52718-02-2P 52719-25-2P 52745-31-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT 21085-72-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with hydroxyestrogens)

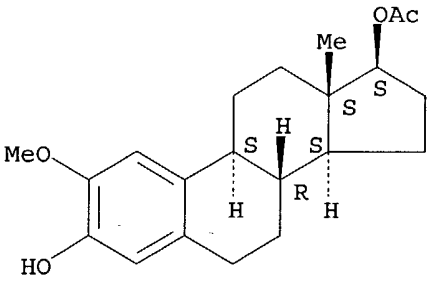
IT 23463-05-0 **52717-98-3** 52717-99-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with methyl bromodeoxyglucopyranuronates)

IT **52717-98-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with methyl bromodeoxyglucopyranuronates)

RN 52717-98-3 HCAPLUS

CN Estra-1,3,5(10)-triene-3,17-diol, 2-methoxy-, 17-acetate, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




=> => d all l26 tot hitstr

L26 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:719252 HCAPLUS

DN 139:224972

ED Entered STN: 14 Sep 2003

TI Synthesis of 2-methoxyestradiol derivatives and uses as antiangiogenic agents

IN **Lavallee, Theresa M.**; **Pribluda, Victor S.**; Simons, Jonathan; Mabjeesh, Nicola; Giannakakou, Paraskevi

PA **Entremed, Inc., USA**

SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K

CC 2-4 (Mammalian Hormones)
Section cross-reference(s): 32

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2003073985 | A2 | 20030912 | WO 2003-US5898 | 20030227 |
| | WO 2003073985 | A3 | 20031231 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-361267P P 20020301

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---|---|---|
| WO 2003073985 | ICM | A61K |

AB Compns. and methods for treating mammalian disease characterized by undesirable angiogenesis and for controlling a number of angiogenesis-related events, conditions, or substances, by administering derivs. of 2-methoxyestradiol of general formula (I) wherein the variables are defined in the specification.

ST estrogen methoxyestradiol analogs angiogenesis inhibitor VEGF DR5 HIFalpha

IT Apoptosis
(2-ME2-induced; synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT Cytokine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DR5 (death receptor 5); synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HIF-1α (hypoxia-inducible factor 1α); synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT Blood vessel
(endothelium; synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT Transcriptional regulation
(of HIF-1α, 2-ME2-inhibited; synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT Angiogenesis
Angiogenesis inhibitors
Human
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT Estrogens
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT 127464-60-2, Vascular Endothelial Growth Factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT 362-07-2DP, 2-Methoxyestradiol, derivs. and analogs 362-07-2P, 2-Methoxyestradiol
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT 50-00-0, Formaldehyde, reactions 50-28-2D, Estradiol, derivs. and analogs 53-16-7, Estrone, reactions 64-18-6, Formic acid, reactions 64-19-7, Acetic acid, reactions 67-68-5, Methyl sulfoxide, reactions

68-12-2, DMF, reactions 71-36-3, 1-Butanol, reactions 75-09-2, Methylene chloride, reactions 79-37-8, Oxalyl chloride 100-39-0, Benzyl bromide 106-95-6, Allyl bromide, reactions 109-99-9, THF, reactions 111-46-6, Diethylene glycol, reactions 121-44-8, Triethylamine, reactions 141-78-6, Ethyl acetate, reactions 302-01-2, Hydrazine, reactions 362-08-3, 2-Methoxyestrone 362-08-3D, 2-Methoxyestrone, olefin analogs 584-08-7, Potassium carbonate 1157-87-5, AH3 1530-32-1, Ethyl triphenylphosphonium bromide 1779-49-3, Methyltriphenylphosphonium bromide 1779-51-7, Butyl triphenylphosphonium bromide 4111-54-0, Lithium diisopropyl amide 4784-77-4, Crotyl bromide 5815-08-7, tert-Butoxy bis(dimethylamino)methane 6228-47-3, Propyl triphenylphosphonium bromide 7447-41-8, Lithium chloride, reactions 7632-00-0, Sodium nitrite 7693-26-7, Potassium hydride 16853-85-3, Lithium aluminum hydride 17455-13-9, 18-Crown-6 17640-15-2, Methyl cyanoformate 41233-93-6, Potassium-tert-amylate 431901-79-0 431901-81-4 431901-84-7 431901-85-8 431901-89-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

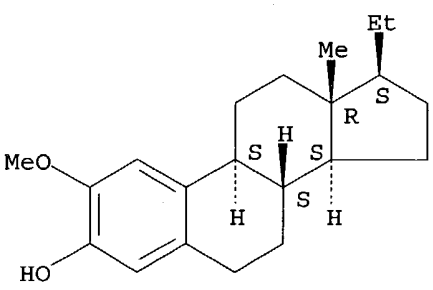
IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT 362-07-2DP, 2-Methoxyestradiol, alkyl analogs 4953-96-2P 6298-51-7P 6301-87-7P 6599-97-9P 7291-57-8P 10332-20-4P 26356-54-7DP, alkyl derivs 26356-54-7DP, alkyl derivs. 26356-54-7P 26357-07-3DP, 16α-alkyl derivs. 26357-07-3P 32162-96-2P 34111-53-0P 93949-26-9P 165619-07-8P **229486-18-4P 431901-68-7P 431901-69-8P 431901-70-1P 431901-71-2P 431901-72-3P 431901-77-8P 431901-78-9P** 431901-80-3DP, alkyl derivs. 431901-89-2DP, alkyl analogs 431901-90-5P 431901-91-6P 431901-92-7P 431901-93-8P 431901-98-3P 431901-99-4P 431902-01-1P 431902-02-2P 431902-03-3P 431902-04-4P 431902-05-5P 431902-06-6P 431902-09-9P 438044-30-5P 464924-32-1P 594873-85-5P 594873-86-6P **594873-87-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

IT **229486-18-4P 431901-68-7P 431901-69-8P 431901-70-1P 431901-71-2P 431901-72-3P 431901-77-8P 431901-78-9P 594873-87-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of 2-methoxyestradiol derivs. and uses as antiangiogenic agents)

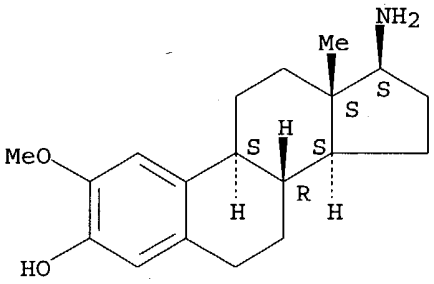
RN 229486-18-4 HCAPLUS
CN 19-Norpregna-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



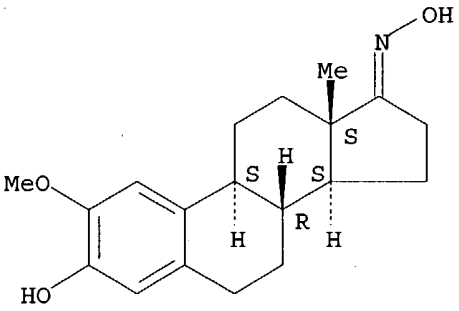
RN 431901-68-7 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 17-amino-2-methoxy-, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



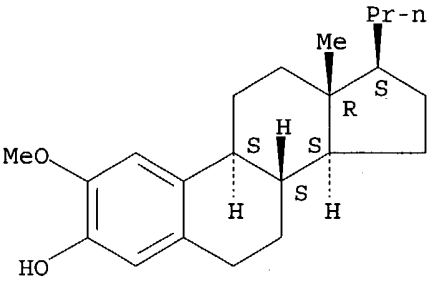

RN 431901-69-8 HCAPLUS
CN Estra-1,3,5(10)-trien-17-one, 3-hydroxy-2-methoxy-, oxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



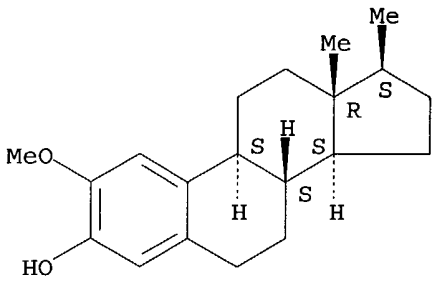

RN 431901-70-1 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propyl-, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



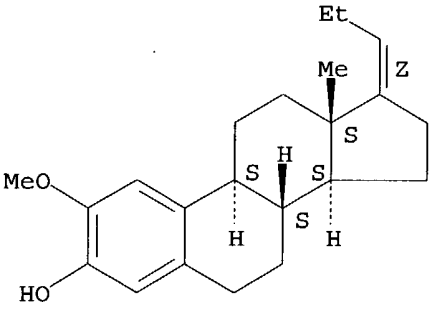

RN 431901-71-2 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methyl-, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



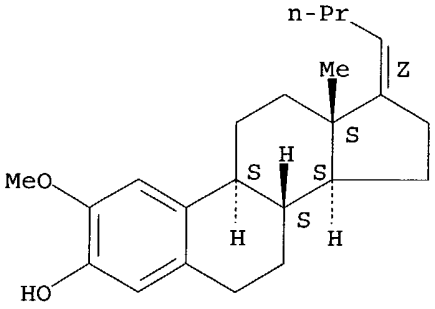

RN 431901-72-3 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propylidene-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



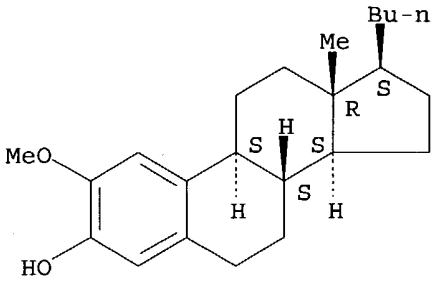

RN 431901-77-8 HCAPLUS
CN 19,21-Dinorchola-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



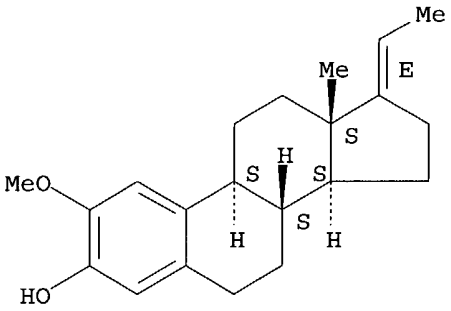

RN 431901-78-9 HCAPLUS
CN 19,21-Dinorchola-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




RN 594873-87-7 HCAPLUS
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.




L26 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:488275 HCAPLUS
DN 137:47357
ED Entered STN: 28 Jun 2002
TI Preparation of 2-methoxyestradiol derivatives as antiangiogenic agents
IN **Agoston, Gregory E.; Shah, Jamshed H.; Hunsucker, Kimberly A.; Pribluda, Victor S.; Lavallee, Theresa M.; Green, Shawn J.; Herbstritt, Christopher J.; Zhan, Xiaoguo H.; Treston, Anthony M.**
PA USA
SO U.S. Pat. Appl. Publ., 37 pp., Cont.-in-part of U. S. Ser. No. 933,894.
CODEN: USXXCO
DT Patent
LA English
IC ICM C07J041-00
ICS C07J043-00; C07J001-00; A61K031-704; A61K031-58; A61K031-56; C07C247-00; A61K031-655; C07J009-00
NCL 552544000
CC 32-3 (Steroids)
Section cross-reference(s): 1
FAN.CNT 2

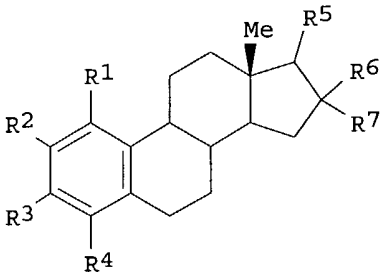
| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | US 2002082433 | A1 | 20020627 | US 2001-939208 | 20010824 <-- |
| PRAI | US 2000-641327 | A2 | 20000818 | | |
| | US 2000-253385P | P | 20001127 | | |
| | US 2000-255302P | P | 20001213 | | |
| | US 2001-278250P | P | 20010323 | | |
| | US 2001-933894 | A2 | 20010821 | | |

CLASS

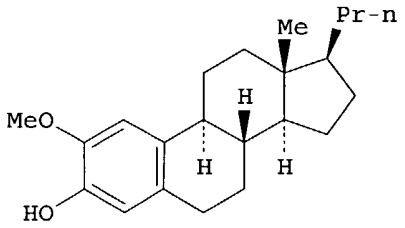
| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---|---|---|
| US 2002082433 | ICM | C07J041-00 |
| | ICS | C07J043-00; C07J001-00; A61K031-704; A61K031-58; A61K031-56; C07C247-00; A61K031-655; C07J009-00 |
| | NCL | 552544000 |

OS MARPAT 137:47357

GI




I




II

AB 2-Methoxyestradiol derivs. of formula I [R1, R4 = H, halo, CN, alkyl, OH, NH2, etc.; R2 = N3, CN, OMe, alkenyl, alkynyl, alkoxy, NH2, etc.; R3 = OH, OAc; R5 = alkyl, alkenyl, (di)alkylamino, OH, alkylene, etc.; R6, R7 = H, alkyl, alkenyl, alkynyl, halo, etc.] are prepared for treating mammalian disease characterized by undesirable angiogenesis. Thus, II was prepared from 2-methoxyestradiol and propyltriphenylphosphonium bromide. The IC50 of II against MDA-MB-231 breast tumor cells was 51.31 μM.

ST methoxyestradiol deriv prepn antiangiogenic; estradiol deriv prepn antiangiogenic; antitumor methoxyestradiol deriv prepn; antimitotic methoxyestradiol deriv prepn

IT Structure-activity relationship
(antitumor; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Mitosis
(inhibitors; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Angiogenesis inhibitors
Antitumor agents
Human
Mammary gland, neoplasm
Neoplasm
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 362-07-2, 2-Methoxyestradiol
RL: PAC (Pharmacological activity); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol 6301-87-7P **431901-72-3P** **431901-73-4P** **431901-75-6P** **431901-77-8P** 431901-91-6P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 1818-12-8P 4953-96-2P 6298-51-7P 6599-97-9P 7291-57-8P 10332-20-4P 32162-96-2P 41259-43-2P 94440-60-5P 165619-07-8P 165881-61-8P **229486-18-4P** **431901-68-7P** **431901-69-8P** **431901-70-1P** **431901-71-2P**

**431901-74-5P 431901-78-9P** 431901-87-0P 431901-90-5P
431901-92-7P 431901-93-8P 431901-94-9P 431901-95-0P 431901-96-1P
431901-97-2P 431901-98-3P 431901-99-4P 431902-00-0P 431902-01-1P
431902-02-2P 431902-03-3P 431902-04-4P 431902-05-5P 431902-06-6P
431902-07-7P 431902-08-8P 431902-09-9P **438044-29-2P**
438044-30-5P 438044-35-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

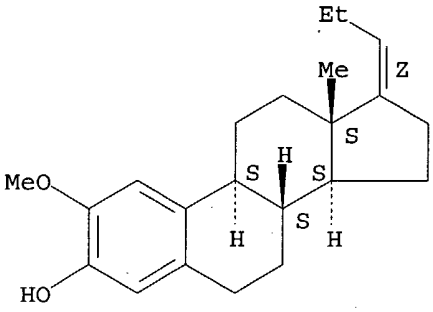
IT 53-16-7, Estrone, reactions 106-95-6, Allyl bromide, reactions
1779-51-7, Butyltriphenylphosphonium bromide 4784-77-4, Crotyl bromide
5815-08-7 6228-47-3, Propyltriphenylphosphonium bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 26356-54-7P 26357-07-3P 93949-26-9P 431901-79-0P 431901-81-4P
431901-82-5P 431901-83-6P 431901-84-7P 431901-85-8P 431901-89-2P
438044-31-6P 438044-32-7P 438044-33-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT **431901-72-3P 431901-73-4P 431901-75-6P**
**431901-77-8P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

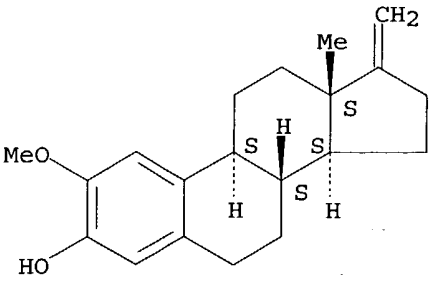
RN 431901-72-3 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propylidene-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



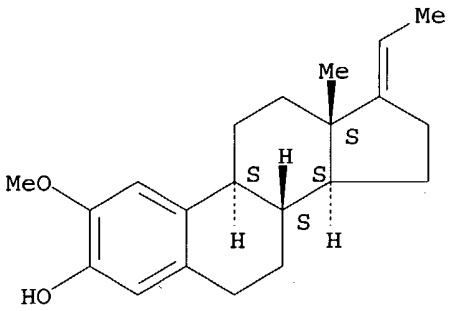

RN 431901-73-4 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



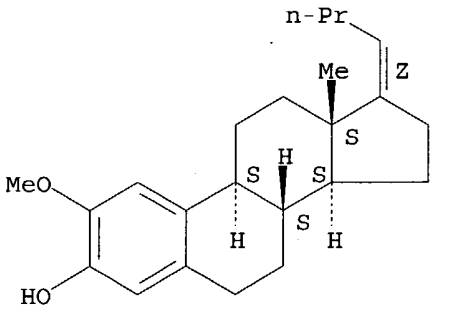
RN 431901-75-6 HCAPLUS
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



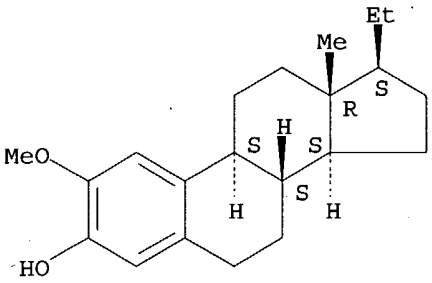

RN 431901-77-8 HCAPLUS
CN 19,21-Dinorchola-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



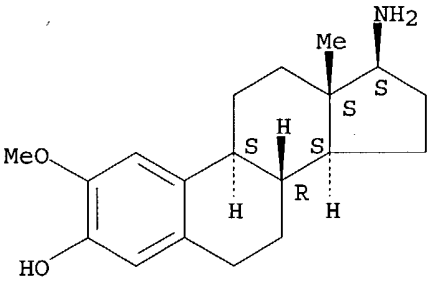

IT **229486-18-4P 431901-68-7P 431901-69-8P**
**431901-70-1P 431901-71-2P 431901-74-5P**
**431901-78-9P 438044-29-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)
RN 229486-18-4 HCAPLUS
CN 19-Norpregna-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



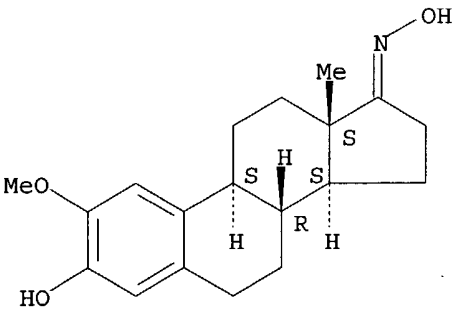

RN 431901-68-7 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 17-amino-2-methoxy-, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



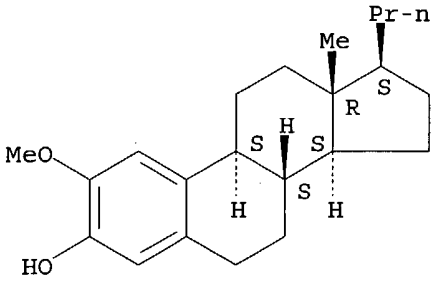

RN 431901-69-8 HCAPLUS
CN Estra-1,3,5(10)-trien-17-one, 3-hydroxy-2-methoxy-, oxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



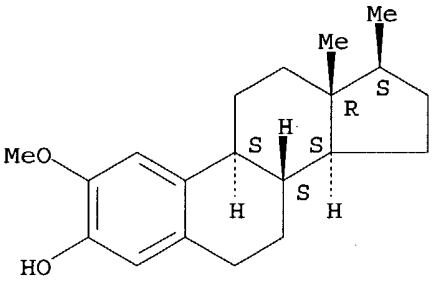

RN 431901-70-1 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propyl-, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



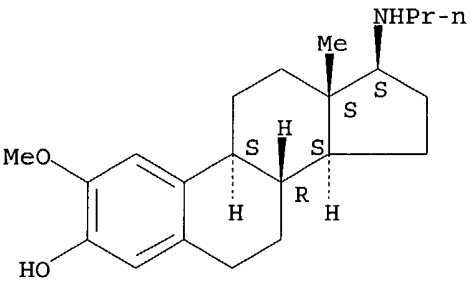

RN 431901-71-2 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methyl-, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



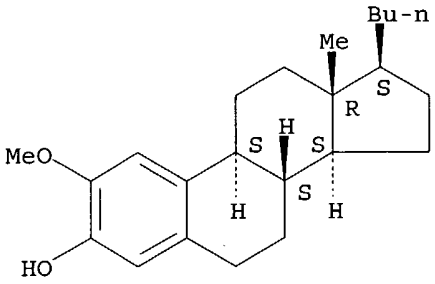

RN 431901-74-5 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-(propylamino)-, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



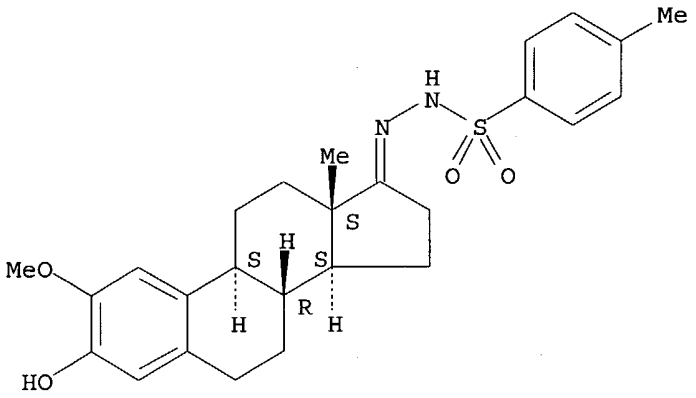

RN 431901-78-9 HCAPLUS
CN 19,21-Dinorchola-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




RN 438044-29-2 HCAPLUS
CN Benzenesulfonic acid, 4-methyl-, (3-hydroxy-2-methoxyestra-1,3,5(10)-trien-17-ylidene)hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.




L26 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:408687 HCAPLUS
DN 137:6309
ED Entered STN: 31 May 2002
TI Preparation of 2-methoxyestradiol analogs as antiangiogenic agents
IN **Agoston, Gregory; Shah, Jamshed H.; Hunsucker, Kimberly A.; Pribluda, Victor; Lavallee, Theresa M. ; Green, Shawn J.; Herbstritt, Christopher J.; Zhan, Xiaoguo H.; Treston, Anthony**
PA **Entremed, Inc., USA**
SO PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07J001-00
CC 32-3 (Steroids)
Section cross-reference(s): 1, 2, 63
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2002042319 | A2 | 20020530 | WO 2001-US26490 | 20010824 |
| | WO 2002042319 | A3 | 20030313 | | |

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PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

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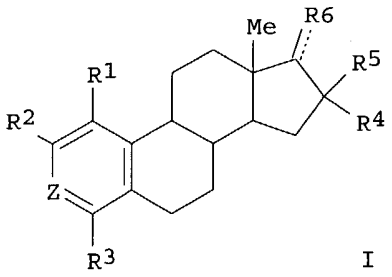
|---|---|---|---|---|---|
| | AU 2001088386 | A5 | 20020603 | AU 2001-88386 | 20010824 |
| | EP 1343803 | A2 | 20030917 | EP 2001-968112 | 20010824 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| PRAI | US 2000-253385P | P | 20001127 | | |
| | US 2000-255302P | P | 20001213 | | |
| | US 2001-278250P | P | 20010323 | | |
| | US 2001-933894 | A | 20010821 | | |
| | WO 2001-US26490 | W | 20010824 | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---|---|---|
| WO 2002042319 | ICM | C07J001-00 |

OS MARPAT 137:6309

GI

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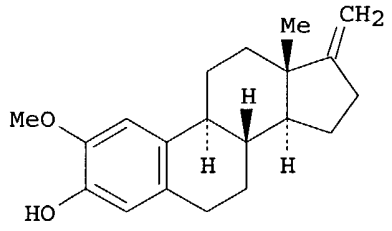


II

AB 2-Methoxyestradiol analogs, such as I [R1, R3 = H, halo, CN, alkyl, OH, CH2OH, NH2, alkylamino; R2 = N3, CN, C.tplbond.CR, C=CHR, C.tplbond.CH, OR, amino; R = H, alkyl; Z = COH, COAc; dashed bond = single bond or double bond; R6 = H, OH, O, oxime, amino, alkyl, alkenyl; R4, R5 = H, alkyl, alkenyl, alkynyl], were prepared for treating mammalian disease characterized by undesirable angiogenesis. Thus, 2-methoxyestradiol analog II was prepared by the reaction of methyltriphenylphosphonium bromide and 2-methoxyestrone. In vitro evaluation against MDA-MB-231 breast tumor cells and HUVEC endothelial cells, II showed IC50 0.24±0 and 0.19±0.19 resp.

ST methoxyestradiol deriv prepn antiangiogenic antitumor; estradiol methoxy deriv prepn antiangiogenic antitumor

IT Cell proliferation
(inhibition; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Mammary gland, neoplasm
(inhibitors; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Antitumor agents
(mammary gland; preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Angiogenesis inhibitors
Human
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT Estrogens
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 53-63-4P, Estra-1,3,5(10)-trien-3-ol **431901-72-3P**
**431901-73-4P 431901-75-6P 431901-77-8P**
431901-83-6P 431901-89-2P 431901-91-6P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 1818-12-8P 4953-96-2P 6298-51-7P 6301-87-7P 6599-97-9P
7291-57-8P 10332-20-4P 32162-96-2P 41259-43-2P 94440-60-5P
165619-07-8P 165881-61-8P 192062-02-5P **229486-18-4P**
**431901-68-7P 431901-69-8P 431901-70-1P**
**431901-71-2P 431901-74-5P** 431901-76-7P
**431901-78-9P** 431901-82-5P 431901-84-7P 431901-86-9P
431901-87-0P 431901-88-1P 431901-92-7P 431901-93-8P 431901-94-9P
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431902-00-0P 431902-01-1P 431902-02-2P 431902-03-3P 431902-04-4P
431902-05-5P 431902-06-6P 431902-07-7P 431902-08-8P 431902-09-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

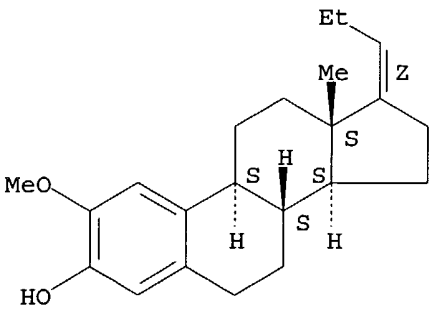
IT 53-16-7, Estrone, reactions 64-18-6, Formic acid, reactions 100-39-0, Benzyl bromide 106-95-6, Allyl bromide, reactions 362-07-2, 2-Methoxyestradiol 1530-32-1, Ethyl triphenylphosphonium bromide 1779-49-3, Methyl triphenylphosphonium bromide 1779-51-7, Butyl triphenylphosphonium bromide 4784-77-4, Crotyl bromide 5815-08-7, tert-Butoxy bis(dimethylamino)methane 6228-47-3, Propyl triphenylphosphonium bromide 17640-15-2, Methyl cyanoformate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT 26356-54-7P 26357-07-3P 93949-26-9P 431901-79-0P 431901-80-3P
431901-81-4P 431901-85-8P 431901-90-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

IT **431901-72-3P 431901-73-4P 431901-75-6P**
**431901-77-8P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

RN 431901-72-3 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propylidene-, (17Z)- (9CI) (CA INDEX NAME)

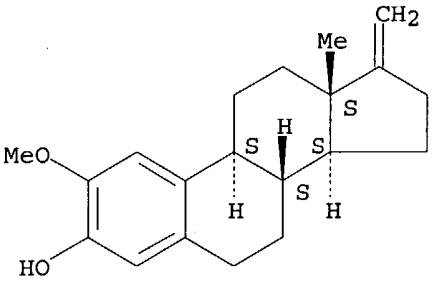
Absolute stereochemistry.
Double bond geometry as shown.




RN 431901-73-4 HCAPLUS

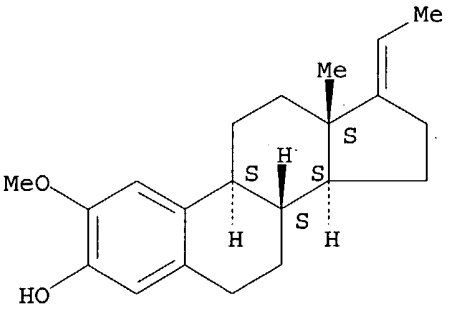
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



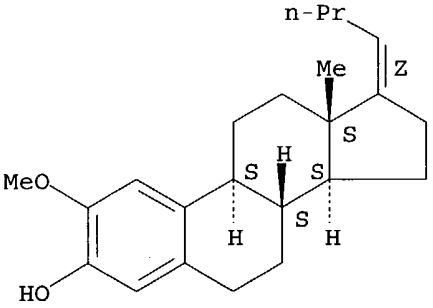

RN 431901-75-6 HCAPLUS
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.




RN 431901-77-8 HCAPLUS
CN 19,21-Dinorchola-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

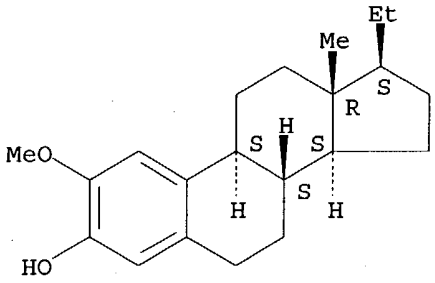
Absolute stereochemistry.
Double bond geometry as shown.




IT **229486-18-4P 431901-68-7P 431901-69-8P 431901-70-1P 431901-71-2P 431901-74-5P 431901-78-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)

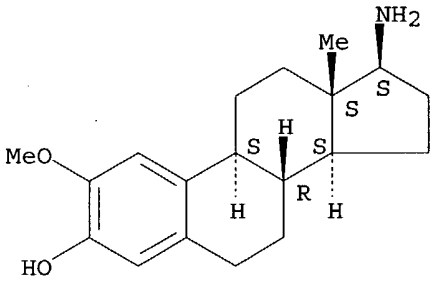
RN 229486-18-4 HCAPLUS
CN 19-Norpregna-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



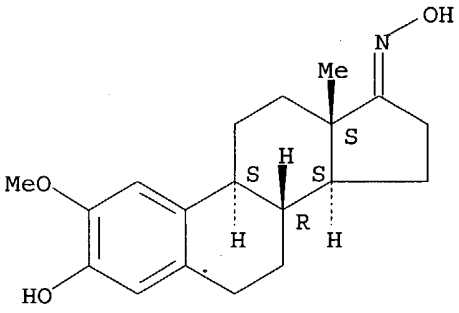

RN 431901-68-7 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 17-amino-2-methoxy-, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



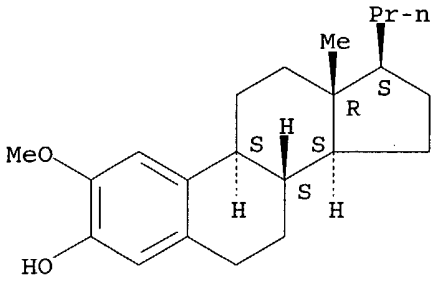

RN 431901-69-8 HCAPLUS
CN Estra-1,3,5(10)-trien-17-one, 3-hydroxy-2-methoxy-, oxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



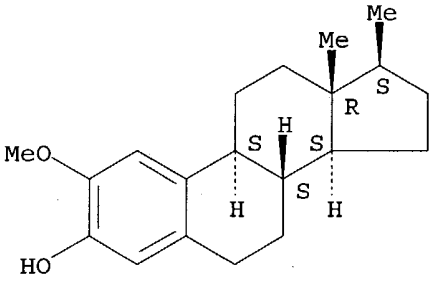

RN 431901-70-1 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propyl-, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



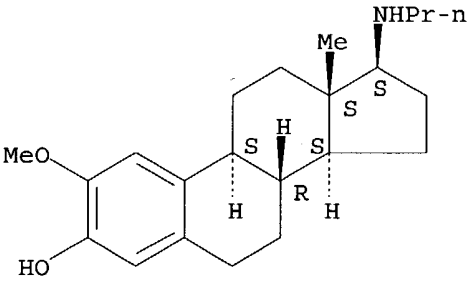

RN 431901-71-2 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methyl-, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



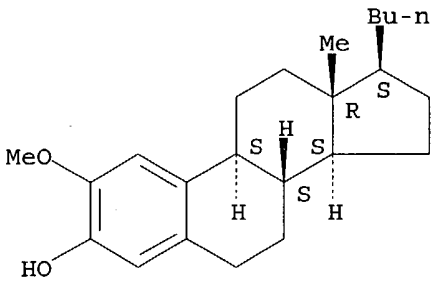

RN 431901-74-5 HCAPLUS
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-(propylamino)-, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




RN 431901-78-9 HCAPLUS
CN 19,21-Dinorchola-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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L28  ANSWER 1 OF 4  USPATFULL on STN
AN     2004:2032  USPATFULL
TI     Systems and methods for rapid evaluation and design of molecules for
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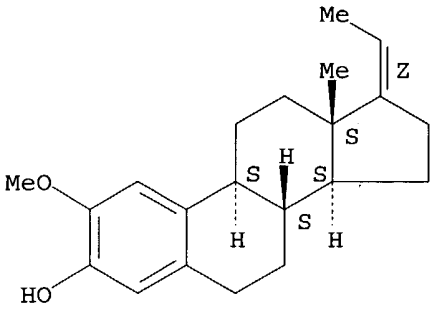
PI     US 2004002052      A1   20040101
AI     US 2002-279546     A1   20021023 (10)
PRAI   US 2001-344560P     20011023 (60)
       US 2001-339954P     20011210 (60)
DT     Utility
FS     APPLICATION
LREP   JOHN S. PRATT, ESQ, KILPATRICK STOCKTON, LLP, 1100 PEACHTREE STREET,
       SUITE 2800, ATLANTA, GA, 30309
CLMN   Number of Claims: 38
ECL    Exemplary Claim: 1
DRWN   16 Drawing Page(s)
LN.CNT 2883
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB     The computer-based systems and methods are for rapidly evaluating
       molecules for suspected biological activity and relative potency, and
       for designing molecules for desired biological activity. The systems and
       methods enable rapid screening of large molecular databases using one or
       more search engines designed to identify molecules predicted to possess
       specific biological activities.

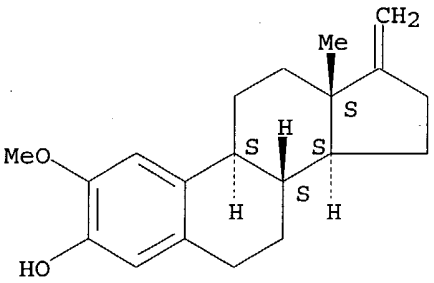
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT   229486-17-3 431901-73-4
        (as standard in construction of search engine for evaluation of substances
        for predicted antiangiogenic activity; systems and methods for rapid
        evaluation and design of mols. for predicted biol. activity)
RN   229486-17-3  USPATFULL
CN   19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI)  (CA
       INDEX NAME)

       Absolute stereochemistry.
       Double bond geometry as shown.
```




RN 431901-73-4 USPATFULL
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

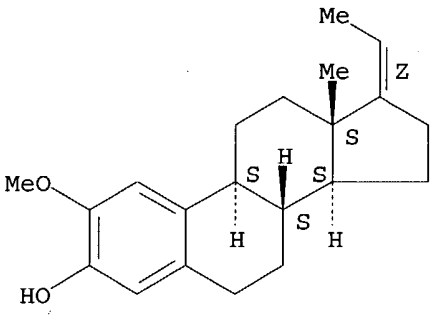



L28 ANSWER 2 OF 4 USPATFULL on STN
AN 2003:226354 USPATFULL
TI 2-substituted pregna-1,3,5(10) triene and chola-1,3,5(10) triene derivatives and their biological activity
IN Hesse, Robert Henry, Winchester, MA, UNITED STATES
Setty, Sundara Katugam Srinivasasetty, Cambridge, MA, UNITED STATES
Pechet, Maurice Murdoch, Cambridge, MA, UNITED STATES
Gile, Michael, Methuen, MA, UNITED STATES
PI US 2003158167 A1 20030821
AI US 2003-275257 A1 20030313 (10)
WO 2001-GB2103 20010511
DT Utility
FS APPLICATION
LREP BACON & THOMAS, PLLC, 625 SLATERS LANE, FOURTH FLOOR, ALEXANDRIA, VA, 22314
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 978
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of formula (I) in which: R.sup.1 represents a hydrogen atom or an O-protecting group; R.sup.2 represents a hydroxyl, lower alkoxy, carboxaldehyde, lower alk-1-enyl or hydroxy- or lower alkoxy-substituted lower alkyl group; R.sup.3 represents a methyl group having α- or β-configuration; X represents a C.sub.1-3 alkylene group or a valence bond; Y represents a carboxaldehyde group or a group of formula --C(R.sup.4)(R.sup.5)OR.sup.1 where R.sup.1 is as defined above and R.sup.4 and R.sup.5, which may be the same or different, are each selected from hydrogen atoms, alkyl, alkenyl and alkynyl groups such that the total carbon content of R.sup.4 and R.sup.5 does not exceed three atoms, with the proviso that X is a valence bond when both R.sup.4

and R.sup.5 are other than hydrogen; and the dotted line signifies that a double bond may optionally be present at the 16(17)-position exhibit potent cell modulating activity, including antiproliferative and antiangiogenic effects.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **229486-17-3P**
(preparation of 2-substituted pregnatriene and cholatriene derivs. with antiproliferative and antiangiogenic activity)
RN 229486-17-3 USPATFULL
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

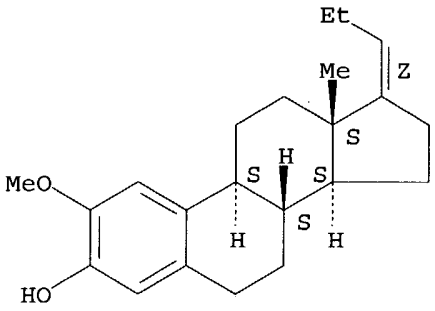



L28 ANSWER 3 OF 4 USPATFULL on STN
AN 2002:157823 USPATFULL
TI Antiangiogenic agents
IN Agoston, Gregory E., Germantown, MD, UNITED STATES
Shah, Jamshed H., Brookeville, MD, UNITED STATES
Hunsucker, Kimberly A., Germantown, MD, UNITED STATES
Pribluda, Victor S., Silver Spring, MD, UNITED STATES
LaVallee, Theresa M., Rockville, MD, UNITED STATES
Green, Shawn J., Vienna, VA, UNITED STATES
Herbstritt, Christopher J., Rockville, VA, UNITED STATES
Zhan, Xiaoguo H., Montgomery Village, MD, UNITED STATES
Treston, Anthony M., Rockville, MD, UNITED STATES
PI US 2002082433 A1 20020627
AI US 2001-939208 A1 20010824 (9)
RLI Continuation-in-part of Ser. No. US 2001-933894, filed on 21 Aug 2001, PENDING Continuation-in-part of Ser. No. US 2000-641327, filed on 18 Aug 2000, PENDING
PRAI US 2000-253385P 20001127 (60)
US 2000-255302P 20001213 (60)
US 2001-278250P 20010323 (60)
DT Utility
FS APPLICATION
LREP John S. Pratt, KILPATRICK STOCKTON LLP, Suite 2800, 1100 Peachtree Street, Atlanta, GA, 30309-4530
CLMN Number of Claims: 92
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2637
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions and methods for treating mammalian disease characterized by undesirable angiogenesis by administering derivatives of 2-methoxyestradiol of the general formula: ##STR1##

wherein the variables are defined in the specification.

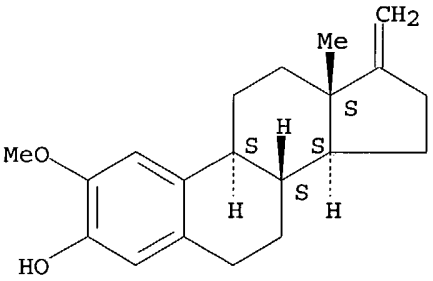
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **431901-72-3P 431901-73-4P 431901-75-6P**
**431901-77-8P**
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)
RN 431901-72-3 USPATFULL
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propylidene-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



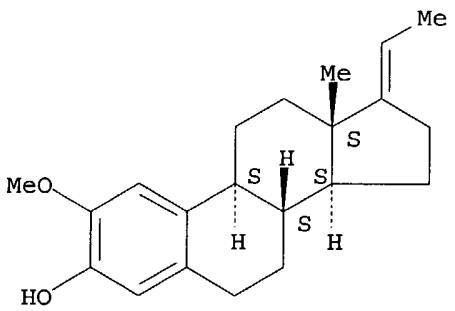

RN 431901-73-4 USPATFULL
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methylene- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



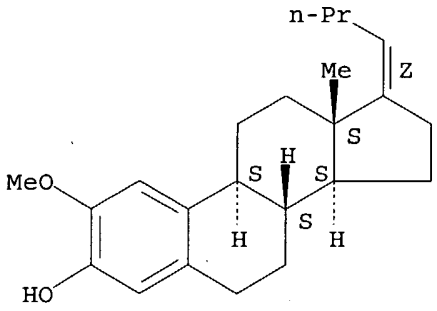

RN 431901-75-6 USPATFULL
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



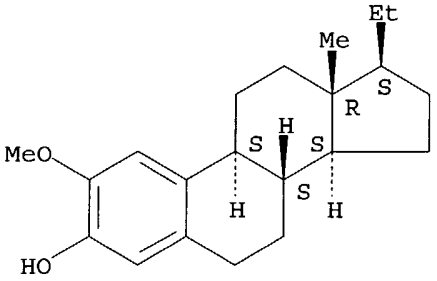
RN 431901-77-8 USPATFULL
CN 19,21-Dinorchola-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



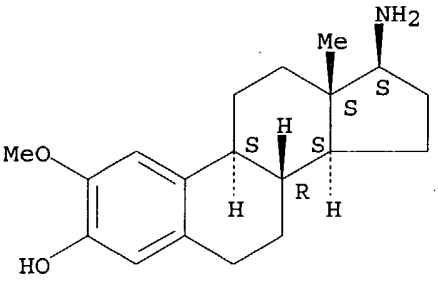

IT **229486-18-4P 431901-68-7P 431901-69-8P**
**431901-70-1P 431901-71-2P 431901-74-5P**
**431901-78-9P 438044-29-2P**
(preparation of 2-methoxyestradiol derivs. as antiangiogenic agents)
RN 229486-18-4 USPATFULL
CN 19-Norpregna-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



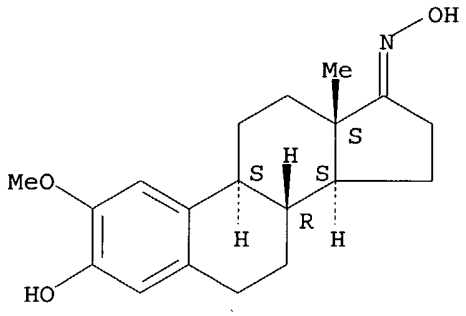

RN 431901-68-7 USPATFULL
CN Estra-1,3,5(10)-trien-3-ol, 17-amino-2-methoxy-, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



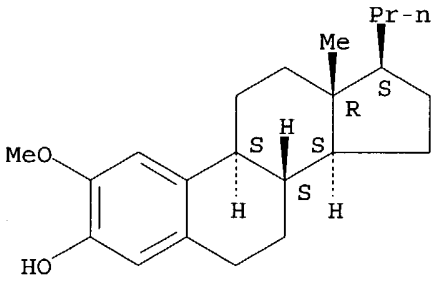

RN 431901-69-8 USPATFULL
CN Estra-1,3,5(10)-trien-17-one, 3-hydroxy-2-methoxy-, oxime (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



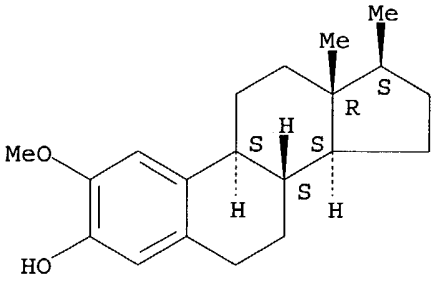

RN 431901-70-1 USPATFULL
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-propyl-, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



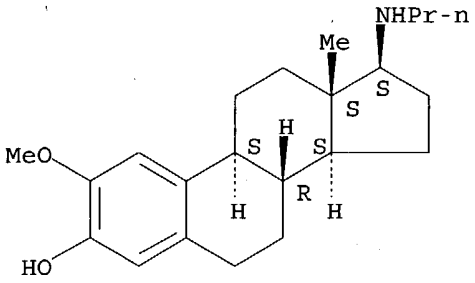

RN 431901-71-2 USPATFULL
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-methyl-, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



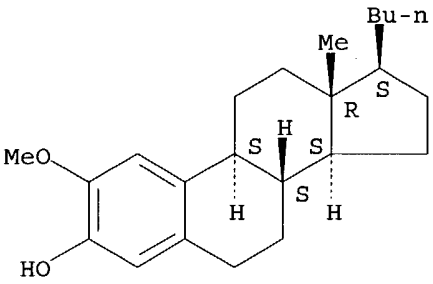

RN 431901-74-5 USPATFULL
CN Estra-1,3,5(10)-trien-3-ol, 2-methoxy-17-(propylamino)-, (17β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



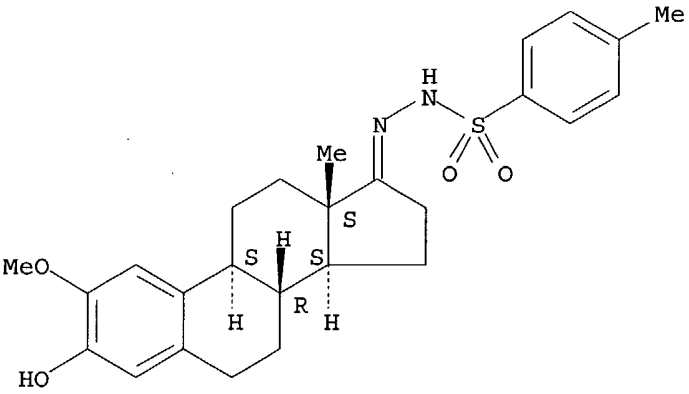

RN 431901-78-9 USPATFULL
CN 19,21-Dinorchola-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.




RN 438044-29-2 USPATFULL
CN Benzenesulfonic acid, 4-methyl-, (3-hydroxy-2-methoxyestra-1,3,5(10)-trien-17-ylidene)hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

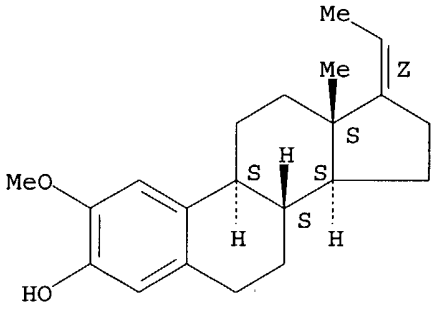



L28 ANSWER 4 OF 4 USPATFULL on STN
AN 2000:41031 USPATFULL
TI Estrone sulfamate inhibitors of estrone sulfatase, and associated pharmaceutical compositions and methods of use
IN Tanabe, Masato, Palo Alto, CA, United States
Peters, Richard H., San Jose, CA, United States
Chao, Wan-Ru, Sunnyvale, CA, United States
Shigeno, Kazuhiko, Saitama, CA, United States
PA SRI International, Menlo Park, CA, United States (U.S. corporation)

PI US 6046186 20000404
AI US 1997-997416 19971224 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Raymond, Richard L.; Assistant Examiner: Coleman, Brenda
LREP Reed, Dianne E.Reed & Associates
CLMN Number of Claims: 65
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3007
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel compounds useful as inhibitors of estrone sulfatase are provided. The compounds have the structural formula (I) wherein r1 is an optional double bond, R.sup.1 and R.sup.2 are selected from the group consisting of hydrogen and lower alky, or together form a cyclic substituent (II) ##STR1## wherein Q is NH, O or CH.sub.2, and the other various substituents are as defined herein. Pharmaceutical compositions and methods for using the compounds of formula (I) to treat estrogen-dependent disorders are provided as well.

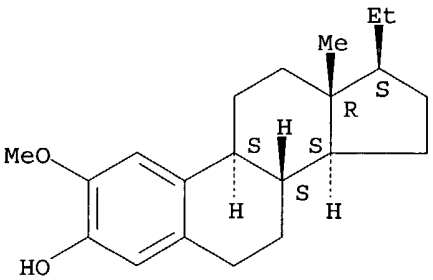
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **229486-17-3P 229486-18-4P**
(preparation of estrone sulfamates as inhibitors of estrone sulfatase)
RN 229486-17-3 USPATFULL
CN 19-Norpregna-1,3,5(10),17(20)-tetraen-3-ol, 2-methoxy-, (17Z)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.




RN 229486-18-4 USPATFULL
CN 19-Norpregna-1,3,5(10)-trien-3-ol, 2-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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     FILE 'HCAPLUS' ENTERED AT 13:43:29 ON 28 OCT 2004
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               SEL RN

     FILE 'REGISTRY' ENTERED AT 13:43:37 ON 28 OCT 2004
L2            68 S E1-E68
L3            63 S L2 AND C5-C6-C6-C6/ES
L4            19 S L3 AND 2/O
L5             1 S L4 AND C20H26O2
               E C20H26O2/MF
L6           146 S E3 AND 4432.3.65/RID
L7           146 S L6 AND 4/NR
L8             2 S L7 AND 2 METHOXY
L9             STR
L10            0 S L9 CSS SAM
L11           12 S L9 SAM
L12          234 S L9 FUL
               SAV TEMP QAZI939/A L12
L13           32 S L9 CSS FUL SUB=L12
               SAV TEMP L13 QAZI939A/A
L14           12 S L2 AND L13
L15           20 S L13 NOT L14
L16            3 S L15 AND (C21H28O4 OR C21H28O2)

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L18            2 S L16
               SEL AN
               EDIT E1-E2 /OR
               EDIT /AN /OREF

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L19            3 S E1-E2
L20            2 S L19 NOT MAZUR ?/AU
L21            6 S L14
L22           11 S L16
L23           15 S L20-L22
L24            3 S L23 AND (AGOSTON G? OR SHAH J? OR HUNSUCKER K? OR PRIBLUDA V?
L25            2 S L23 AND ENTREMED?/PA,CS
L26            3 S L1,L24,L25
L27           12 S L23 NOT L26

     FILE 'USPATFULL, USPAT2' ENTERED AT 14:03:09 ON 28 OCT 2004
L28            4 S L14 OR L16

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     FILE 'HCAOLD' ENTERED AT 14:03:52 ON 28 OCT 2004

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L29            1 S L20 AND L21,L22
L30            2 S L20,L29
L31           10 S L27 NOT L30

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